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| NEWS | 1 | | Web Page for STN Seminar Schedule - N. America |
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| NEWS | 3 | AUG 06 | FSTA enhanced with new thesaurus edition |
| NEWS | 4 | AUG 13 | CA/CAplus enhanced with additional kind codes for granted patents |
| NEWS | 5 | AUG 20 | CA/CAplus enhanced with CAS indexing in pre-1907 records |
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| NEWS | 15 | OCT 02 | CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt |
| NEWS | 16 | OCT 19 | BEILSTEIN updated with new compounds |
| NEWS | 17 | NOV 15 | Derwent Indian patent publication number format enhanced |
| NEWS | 18 | NOV 19 | WPIX enhanced with XML display format |
| NEWS | 19 | NOV 30 | ICSD reloaded with enhancements |
| NEWS | 20 | DEC 04 | LINPADOCDB now available on STN |
| NEWS | 21 | DEC 14 | BEILSTEIN pricing structure to change |
| NEWS | 22 | DEC 17 | USPATOLD added to additional database clusters |
| NEWS | 23 | DEC 17 | IMSDRUGCONF removed from database clusters and STN |
| NEWS | 24 | DEC 17 | DGENE now includes more than 10 million sequences |
| NEWS | 25 | DEC 17 | TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment |
| NEWS | 26 | DEC 17 | MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary |
| NEWS | 27 | DEC 17 | CA/CAplus enhanced with new custom IPC display formats |
| NEWS | 28 | DEC 17 | STN Viewer enhanced with full-text patent content from USPATOLD |
| NEWS | 29 | JAN 02 | STN pricing information for 2008 now available |
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NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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                                                             ENTRY    SESSION
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DICTIONARY FILE UPDATES:  21 JAN 2008  HIGHEST RN 1000370-19-3

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=> e methy-th
E1         170     METHUSELAH/BI
E2        1596     METHY/BI
E3           0 --> METHY-TH/BI
E4           1     METHYB/BI
E5           1     METHYBOL/BI
E6           1     METHYBROM/BI
E7           3     METHYCAINE/BI
E8           1     METHYCILLIN/BI
E9           1     METHYCLO/BI
E10          1     METHYCLOTHI/BI
E11          1     METHYCLOTHIAZI/BI
E12          1     METHYCLOTHIAZID/BI

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|---|---|---|
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FILE LAST UPDATED: 21 Jan 2008 (20080121/ED)

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They are available for your review at:

http://www.cas.org/infopolicy.html

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=> s (ido or 1mt or indoleamine) and inhibitor
          1168 IDO
            22 IDOS
          1187 IDO
                 (IDO OR IDOS)
            32 1MT
          1981 INDOLEAMINE
           742 INDOLEAMINES
          2344 INDOLEAMINE
                 (INDOLEAMINE OR INDOLEAMINES)
        562807 INHIBITOR
        565010 INHIBITORS
        882264 INHIBITOR
                 (INHIBITOR OR INHIBITORS)
L1         431 (IDO OR 1MT OR INDOLEAMINE) AND INHIBITOR

=> s l1 and (cancer or tumor or neoplasm)
        344399 CANCER
         50644 CANCERS
        357231 CANCER
                 (CANCER OR CANCERS)
        437225 TUMOR
        164827 TUMORS
        488179 TUMOR
                 (TUMOR OR TUMORS)
        479640 NEOPLASM
         36935 NEOPLASMS
        496541 NEOPLASM
                 (NEOPLASM OR NEOPLASMS)
L2         127 L1 AND (CANCER OR TUMOR OR NEOPLASM)

=> s l2 and py<=2003
      23975295 PY<=2003
L3          56 L2 AND PY<=2003
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=> d l3 ibib abs 1-56

L3 ANSWER 1 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:107543 CAPLUS
DOCUMENT NUMBER: 140:252238
TITLE: Inhibition of indoleamine 2,3-dioxygenase suppresses NK cell activity and accelerates tumor growth
AUTHOR(S): Kai, Seiichiro; Goto, Shigeru; Tahara, Kouichirou; Sasaki, Atsushi; Kawano, Katsunori; Kitano, Seigo
CORPORATE SOURCE: Department of Surgery I, Oita University Faculty of Medicine, Oita, 897-5593, Japan
SOURCE: Journal of Experimental Therapeutics and Oncology ( 2003), 3(6), 336-345
CODEN: JETOFX; ISSN: 1359-4117
PUBLISHER: Blackwell Publishing, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO), a tryptophan catabolizing enzyme, is induced under various pathol. conditions, including viral and bacterial infection, allograft rejection, cerebral ischemia, and tumor growth. The authors have previously reported that the expression of IDO mRNA was increased in some clin. cases of hepatocellular carcinoma in which the recurrence-free survival rate in these IDO-pos. patients was higher than that in patients without IDO mRNA induction in tumors. Addnl., IDO expressed in tumors was localized not to the tumor cells but instead to tumor-infiltrating cells by immunohistochem. Here, to elucidate the mechanisms underlying anti-tumor effect of IDO, the authors investigated whether IDO inhibitor (1-methyl-DL-tryptophan, 1MT) affects the growth of s.c. B16 tumors in mice. Subsequently, the activity of natural killer (NK) cells was investigated under the conditions of inhibited IDO activity in vivo and in vitro. IDO mRNA expression of B16 cells, B16 s.c. tumor , splenocytes of mice, and human NK cells were studied by reverse transcription-polymerase chain reaction. B16 s.c. tumor growth with or without IDO inhibition was observed and cytotoxic activity of NK cells were investigated under the conditions of inhibited IDO activity in vivo and in vitro. IDO mRNA was expressed in B16 s.c. tumor, splenocytes of tumor bearing mice, co-cultured splenocytes with B16, and human NK cells. On day 14, after injection of B16 melanoma cells, the sizes of tumors in IDO-inhibited mice were larger than those in control mice. The cytotoxic activity of mouse NK cells was reduced by IDO inhibition in vivo. In in vitro inhibition of IDO, NK activity was reduced in dose-dependent manner of 1MT. Thus, IDO plays an important role in anti-tumor immunity by regulating cytotoxic activity of NK cells.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:818069 CAPLUS
DOCUMENT NUMBER: 139:322295
TITLE: Antigen-presenting cell populations and their use as reagents for enhancing or reducing immune tolerance
INVENTOR(S): Mellor, Andrew L.; Munn, David H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2003194803 | A1 | 20031016 | US 2002-121909 | 20020412 <-- |
| CA 2483451 | A1 | 20031023 | CA 2002-2483451 | 20020412 <-- |
| WO 2003087347 | A1 | 20031023 | WO 2002-US11319 | 20020412 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002307243 | A1 | 20031027 | AU 2002-307243 | 20020412 <-- |
| EP 1501918 | A1 | 20050202 | EP 2002-807233 | 20020412 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2006292618 | A1 | 20061228 | US 2006-474162 | 20060623 |
| US 2007048769 | A1 | 20070301 | US 2006-474144 | 20060623 |

PRIORITY APPLN. INFO.: US 2002-121909 A 20020412
WO 2002-US11319 W 20020412

AB The disclosed invention is based on the discovery that antigen-presenting cells (APCs) may be generated to have predetd. levels of expression of the intracellular enzyme, indoleamine 2,3-dioxygenase (IDO ). Because expression of high levels of IDO is correlated with a reduced ability to stimulate T cell responses and an enhanced ability to induce immunol. tolerance, APCs having high levels of IDO may be used to increase tolerance in the immune system, as for example in transplant therapy or treatment of autoimmune disorders. For example, APCs having high levels of IDO, and expressing or loaded with at least one antigen from a donor tissue may be used to increase tolerance of the recipient to the donor's tissue. Alternatively, APCs having reduced levels of IDO expression and expressing or loaded with at least one antigen from a cancer or infectious pathogen may be used as vaccines to promote T cell responses and increase immunity.

L3 ANSWER 3 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:764699 CAPLUS
DOCUMENT NUMBER: 139:322076
TITLE: Evidence for a tumoral immune resistance mechanism based on tryptophan degradation by indoleamine 2,3-dioxygenase
AUTHOR(S): Uyttenhove, Catherine; Pilotte, Luc; Theate, Ivan; Stroobant, Vincent; Colau, Didier; Parmentier, Nicolas; Boon, Thierry; Van den Eynde, Benoit J.
CORPORATE SOURCE: Ludwig Institute for Cancer Research and Cellular Genetics Unit, Universite de Louvain, Brussels, B-1200, Belg.
SOURCE: Nature Medicine (New York, NY, United States) ( 2003), 9(10), 1269-1274
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB T lymphocytes undergo proliferation arrest when exposed to tryptophan shortage, which can be provoked by indoleamine 2,3-dioxygenase (

IDO), an enzyme that is expressed in placenta and catalyzes tryptophan degradation Here we show that most human tumors constitutively express IDO. We also observed that expression of IDO by immunogenic mouse tumor cells prevents their rejection by preimmunized mice. This effect is accompanied by a lack of accumulation of specific T cells at the tumor site and can be partly reverted by systemic treatment of mice with an inhibitor of IDO, in the absence of noticeable toxicity. These results suggest that the efficacy of therapeutic vaccination of cancer patients might be improved by concomitant administration of an IDO inhibitor.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:669428 CAPLUS

DOCUMENT NUMBER: 139:290067

TITLE: Contribution of the MUC1 tandem repeat and cytoplasmic tail to invasive and metastatic properties of a pancreatic cancer cell line

AUTHOR(S): Kohlgraf, Karl G.; Gawron, Andrew J.; Higashi, Michiyo; Meza, Jane L.; Burdick, Michael D.; Kitajima, Shinichi; Kelly, David L.; Caffrey, Thomas C.; Hollingsworth, Michael A.

CORPORATE SOURCE: Department of Pathology and Microbiology, Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, NE, 68198-6805, USA

SOURCE: Cancer Research (2003), 63(16), 5011-5020
CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal

LANGUAGE: English

AB MUC1 is a polymorphic, highly glycosylated, type I transmembrane protein expressed by ductal epithelial cells of many organs including pancreas, breast, gastrointestinal tract, and airway. MUC1 is overexpressed and differentially glycosylated by adenocarcinomas that arise in these organs, and is believed to contribute to invasive and metastatic potential by contributing to cell surface adhesion properties [via the tandem repeat (TR) domain] and through morphogenetic signal transduction via the cytoplasmic tail (CT). The large extracellular TR of MUC1 consists of a heavily glycosylated, 20 amino acid sequence that shows allelic variation with respect to number of repeats. This portion of MUC1 may directly mediate adhesive or antiadhesive interactions with other surface mols. on adjacent cells and through these interactions initiate signal transduction pathways that are transmitted through the CT. We investigated the contribution of the TR domain and the CT of MUC1 to the in vivo invasive and metastatic potential, and the gene expression profile of the human pancreatic tumor cell line S2-013. Results showed that S2-013 cells overexpressing full-length MUC1 displayed a less invasive and metastatic phenotype compared with control-transfected cells and cells expressing MUC1 lacking the TR domain or CT. Clonal populations were analyzed by cDNA array gene expression anal., which showed differences in the gene expression profiles between the different cell lines. Among the genes differentially expressed were several that encode proteins believed to play a role in invasion and metastasis.

REFERENCE COUNT: 79 THERE ARE 79 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:491063 CAPLUS

DOCUMENT NUMBER: 139:57897

TITLE: Novel pharmaceutical composition of interferon gamma or pirfenidone combined with molecular diagnostics for the improved treatment of interstitial lung diseases
INVENTOR(S): Bevec, Dorian; Ziesche, Rolf
PATENT ASSIGNEE(S): Mondobiotech SA, Switz.
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003051388 | A2 | 20030626 | WO 2002-CH691 | 20021212 <-- |
| WO 2003051388 | A3 | 20031030 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2470763 | A1 | 20030626 | CA 2002-2470763 | 20021212 <-- |
| AU 2002347182 | A1 | 20030630 | AU 2002-347182 | 20021212 <-- |
| BR 2002007310 | A | 20040817 | BR 2002-7310 | 20021212 |
| EP 1455813 | A2 | 20040915 | EP 2002-782602 | 20021212 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| CN 1620309 | A | 20050525 | CN 2002-828206 | 20021212 |
| JP 2005528082 | T | 20050922 | JP 2003-552321 | 20021212 |
| NO 2003003642 | A | 20031017 | NO 2003-3642 | 20030815 <-- |
| US 2006270618 | A1 | 20061130 | US 2004-498079 | 20040608 |
| IN 2004DN07852 | A | 20070427 | IN 2004-DN7852 | 20040615 |
| IN 2004DN01679 | A | 20070525 | IN 2004-DN1679 | 20040615 |
| PRIORITY APPLN. INFO.: | | | EP 2001-130011 A | 20011218 |
| | | | WO 2002-CH691 W | 20021212 |

AB The present invention relates to a novel pharmaceutical composition of compds. having the biol. activity of interferon gamma (IFN-γ) or pirfenidone in combination with a diagnostic array of candidate polynucleotides for the improved treatment of all forms of interstitial lung diseases, in particular of idiopathic pulmonary fibrosis (IPF). This invention describes the combination of mol. diagnosis and clin. therapy as a novel medication principle for reduction of mortality and improvement of disease management in interstitial lung diseases.

L3 ANSWER 6 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:355709 CAPLUS
DOCUMENT NUMBER: 138:335902
TITLE: Nucleic acid molecules and proteins for the identification, assessment, prevention, and therapy of ovarian cancer
INVENTOR(S): Monahan, John E.; Gannavarapu, Manjula; Hoersch, Sebastian; Kamatkar, Shubhangi; Kovats, Steven G.; Meyers, Rachel E.; Morrisey, Michael P.; Olandt, Peter J.; Sen, Ami; Veiby, Petter Ole; Mills, Gordon B.; Bast, Robert C.; Lu, Karen; Schmandt, Rosemarie E.; Zhao, Xumei; Glatt, Karen
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 44 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| US 2003087250 | A1 | 20030508 | US 2002-97340 | 20020314 <-- |
| WO 2002071928 | A2 | 20020919 | WO 2002-US7826 | 20020314 <-- |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2002258518 | A1 | 20020924 | AU 2002-258518 | 20020314 <-- |
| US 2005214831 | A1 | 20050929 | US 2005-50926 | 20050204 |

| PRIORITY APPLN. INFO.: | | |
|---|---|---|
| US 2001-276025P | P | 20010314 |
| US 2001-276026P | P | 20010314 |
| US 2001-311732P | P | 20010810 |
| US 2001-323580P | P | 20010919 |
| US 2001-324967P | P | 20010926 |
| US 2001-325102P | P | 20010926 |
| US 2001-325149P | P | 20010926 |
| US 2002-97340 | A1 | 20020314 |
| WO 2002-US7826 | W | 20020314 |

AB The invention relates to newly discovered nucleic acid mols. and proteins associated with ovarian cancer. All OV markers and M352-M360 markers were identified by transcriptional profiling using mRNA from 9 normal ovarian epithelia, 11 stage I/II ovarian cancer tumors, and 25 stage III/IV tumors. Clones having expression ≥2-fold higher in ovarian tumors as compared to their expression in non-ovarian tumor tissues in at least 4 tumor samples were selected. Addnl. Mxxx markers were identified by transcriptional profiling using mRNA from 67 ovarian tumors of various histotypes and stage and 96 non-ovarian tumor tissues including normal ovarian epithelium, benign conditions, other normal tissues, and other abnormal tissues. Clones having expression ≥3-fold higher in at least 10% of ovarian tumors, as compared to their expression in non-ovarian tumor tissue, were designated as ovarian cancer specific markers. Clones were identified by BLAST anal., against both public and proprietary sequence databases, of EST sequences known to be associated with each clone. A total of 363 cDNA markers including their protein products are provided. Compns., kits, and methods for detecting, characterizing, preventing, and treating human ovarian cancers are provided.

L3 ANSWER 7 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:968965 CAPLUS
DOCUMENT NUMBER: 138:88595
TITLE: Tryptophan deprivation sensitizes activated T cells to apoptosis prior to cell division
AUTHOR(S): Lee, Geon Kook; Park, Hyeon Jin; MacLeod, Megan; Chandler, Phillip; Munn, David H.; Mellor, Andrew L.
CORPORATE SOURCE: Program in Molecular Immunology, Institute of Molecular Medicine and Genetics, Medical College of

Georgia, Augusta, GA, 30912, USA
SOURCE: Immunology (2002), 107(4), 452-460
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cells expressing indoleamine 2,3-dioxygenase (IDO), an enzyme which catabolizes tryptophan, prevent T-cell proliferation in vitro, suppress maternal anti-fetal immunity during pregnancy and inhibit T-cell-mediated responses to tumor-associated antigens. To examine the mechanistic basis of these phenomena the authors activated naive murine T cells in chemical defined tryptophan-free media. Under these conditions T cells expressed CD25 and CD69 and progressed through the first 12 h of G0/G1 phase but did not express CD71, cyclin D3, cdk4, begin DNA synthesis, or differentiate into cytotoxic effector cells. In addition, activated T cells with their growth arrested by tryptophan deprivation exhibited enhanced tendencies to die via apoptosis when exposed to anti-Fas antibodies. Apoptosis was inhibited by caspase inhibitor and was not observed when T cells originated from Fas-deficient mice. These findings suggest that T cells activated in the absence of free tryptophan entered the cell cycle but cell cycle progression ceased in mid-G1 phase and T cells became susceptible to death via apoptosis, in part though Fas-mediated signaling. Thus, mature antigen-presenting cells expressing IDO and Fas-ligand may induce antigen-specific T-cell tolerance by blocking T-cell cycle progression and by rapid induction of T-cell activation induced cell death in local tissue microenvironments.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:787505 CAPLUS
DOCUMENT NUMBER: 138:105164
TITLE: Indolamine 2,3-dioxygenase, immunosuppression and pregnancy
AUTHOR(S): Mellor, Andrew L.; Chandler, Phillip; Lee, Geon Kook; Johnson, Theodore; Keskin, Derin B.; Lee, Jeffrey; Munn, David H.
CORPORATE SOURCE: Institute of Molecular Medicine and Genetics, Program in Molecular Immunology, Medical College of Georgia, Augusta, GA, 30912, USA
SOURCE: Journal of Reproductive Immunology (2002), 57(1-2), 143-150
CODEN: JRIMDR; ISSN: 0165-0378
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Pharmacol. inhibition of indolamine 2,3-dioxygenase ( IDO) activity during murine pregnancy results in maternal T-cell-mediated rejection of allogeneic but not syngeneic conceptuses. Increased risk of allogeneic pregnancy failure induced by exposure to IDO inhibitor is strongly correlated with maternal C3 deposition at the maternal-fetal interface. Here we review evidence that cells expressing IDO contribute to immunosuppression by inhibiting T-cell responses to tumor antigens and tissue allografts, as well as fetal tissues.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:674702 CAPLUS
DOCUMENT NUMBER: 137:200238
TITLE: Indoleamine 2,3-dioxygenase contributes to

tumor cell evasion of T cell-mediated rejection

AUTHOR(S): Friberg, Maria; Jennings, Ronald; Alsarraj, Marwan; Dessureault, Sophie; Cantor, Alan; Extermann, Martine; Mellor, Andrew L.; Munn, David H.; Antonia, Scott J.

CORPORATE SOURCE: Department of Interdisciplinary Oncology, H. Lee Moffitt Cancer Center, Tampa, FL, 33612, USA

SOURCE: International Journal of Cancer (2002), 101(2), 151-155
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The priming of an appropriate antitumor T cell response rarely results in the rejection of established tumors. The characteristics of tumors that allow them to evade a T cell-mediated rejection are unknown for many tumors. The authors report on evidence that the expression of the immunosuppressive enzyme, indoleamine 2,3-dioxygenase (IDO) by mononuclear cells that invade tumors and tumor-draining lymph nodes, is a mechanism that may account for this observation. Lewis lung carcinoma (LLC) cells stimulated a more robust allogeneic T cell response in vitro in the presence of a competitive inhibitor of IDO, I-Me tryptophan. When administered in vivo this inhibitor also resulted in delayed LLC tumor growth in syngeneic mice. The authors' study provides evidence for a novel mechanism whereby tumors evade rejection by the immune system, and suggests the possibility that inhibiting IDO may be developed as an anti-cancer immunotherapeutic strategy.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:57331 CAPLUS

DOCUMENT NUMBER: 136:319540

TITLE: Gene profiling reveals unknown enhancing and suppressive actions of glucocorticoids on immune cells

AUTHOR(S): Galon, Jerome; Franchimont, Denis; Hiroi, Naoki; Frey, Gregory; Boettner, Antje; Ehrhart-Bornstein, Monika; O'Shea, John J.; Chrousos, George P.; Bornstein, Stefan R.

CORPORATE SOURCE: Lymphocyte Cell Biology Section, NIAMS, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: FASEB Journal (2002), 16(1), 61-71
CODEN: FAJOEC; ISSN: 0892-6638

PUBLISHER: Federation of American Societies for Experimental Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Glucocorticoids continue to be the major immunomodulatory agents used in clin. medicine today. However, their actions as anti-inflammatory and immunosuppressive drugs are both beneficial and deleterious. We analyzed the effect of glucocorticoids on the gene expression profile of peripheral blood mononuclear cells from healthy donors. DNA microarray anal. combined with quant. TaqMan PCR and flow cytometry revealed that glucocorticoids induced the expression of chemokine, cytokine, and complement family members as well as of newly discovered innate immune-related genes, including scavenger and Toll-like receptors. In contrast, glucocorticoids repressed the expression of adaptive immune-related genes. Simultaneous inhibitory and stimulatory effects of glucocorticoids were found on inflammatory T helper subsets and apoptosis-related gene clusters. In cells activated by T cell receptor

crosslinking, glucocorticoids down-regulated the expression of specific genes that were previously up-regulated in resting cells, suggesting a potential new mechanism by which they exert pos. and neg. effects. Considering the broad and continuously renewed interest in glucocorticoid therapy, the profiles we describe here will be useful in designing more specific and efficient treatment strategies.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:835010 CAPLUS
DOCUMENT NUMBER: 136:16482
TITLE: Norharman, an indoleamine-derived β-carboline, but not Trp-P-2, a γ-carboline, induces apoptotic cell death in human neuroblastoma SH-SY5Y cells
AUTHOR(S): Uezono, T.; Maruyama, W.; Matsubara, K.; Naoi, M.; Shimizu, K.; Saito, O.; Ogawa, K.; Mizukami, H.; Hayase, N.; Shiono, H.
CORPORATE SOURCE: Department of Legal Medicine, Asahikawa Medical College, Asahikawa, Japan
SOURCE: Journal of Neural Transmission (2001), 108(8-9), 943-953
CODEN: JNTRF3; ISSN: 1435-1463
PUBLISHER: Springer-Verlag Wien
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Carbolines, azaheterocyclic amines derived from indoleamines, have various biol. activities, such as neurotoxicity of β-carbolines and potent mutagenicity of γ-carbolines. In this study, structural significance among these carbolines was investigated in relation to the types of cell death, apoptosis and necrosis, using human neuroblastoma SH-SY5Y cells. DNA damage was quant. analyzed by a single-cell gel electrophoresis assay. DNA damage was induced by both β-carbolines, harman and norharman, and γ-carbolines, 3-amino-1,4-dimethyl-5H-pyrido[4,3-b]indole (Trp-P-1) and 3-amino-4-methyl-5H-pyrido[4,3-b]indole (Trp-P-2), in a dose dependent manner. γ-Carbolines were more potent to damage DNA than β-carbolines. Alkaline lysis of the cells prevented DNA damage induced by β-carboline, and pre-treatment of the cells with cycloheximide, an inhibitor of protein synthesis, reduced DNA damage caused by norharman. Morphol. observation showed condensed and fragmented nuclei typical for apoptosis, in the cells treated with norharman. Thus, DNA damage induced by norharman was proved to be apoptotic. However, harman, which had a Me substitution at the position 1, might induce necrosis in the cells. On the other hand, γ-carbolines, Trp-P-1 and Trp-P-2, directly damaged DNA. Thus, the nitrogen atom at the γ-position and/or an amino group in carboline structure would be required to induce the direct DNA cleavage.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 12 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:796060 CAPLUS
DOCUMENT NUMBER: 136:132926
TITLE: Synthesis and release of neurotoxic kynurenine metabolites by human monocyte-derived macrophages
AUTHOR(S): Chiarugi, Alberto; Calvani, Maura; Meli, Elena; Traggiai, Elisabetta; Moroni, Flavio
CORPORATE SOURCE: Department of Preclinical and Clinical Pharmacology, University of Florence, Florence, 50139, Italy
SOURCE: Journal of Neuroimmunology (2001), 120(1-2), 190-198

CODEN: JNRIDW; ISSN: 0165-5728
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors studied the regulation of the kynurenine pathway of tryptophan metabolism in human monocyte-derived macrophages (MDM) with the aim of evaluating macrophage involvement in inflammatory neurol. disorders. Cultured MDM metabolized tryptophan and released kynurenine metabolites, including the excitotoxin quinolinic acid (QUIN). Lipopolysaccharides (LPS) or the pro-inflammatory cytokines INFγ and TNFα increased, while IL 4 or IL 10 inhibited the rate of tryptophan metabolism and the release of QUIN. The incubation media of INFγ-exposed MDM caused neuronal death in primary cultures of mixed cortical cells. Glutamate receptor antagonists or poly(ADP-ribose) polymerase inhibitors significantly reduced this death, thus suggesting new possibilities for the treatment of neuronal damage in neuroinflammatory disorders.
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 13 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:411495 CAPLUS
DOCUMENT NUMBER: 135:179631
TITLE: Profiling changes in gene expression during differentiation and maturation of monocyte-derived dendritic cells using both oligonucleotide microarrays and proteomics
AUTHOR(S): Le Naour, Francois; Hohenkirk, Lyndon; Grolleau, Annabelle; Misek, David E.; Lescure, Pascal; Geiger, James D.; Hanash, Samir; Beretta, Laura
CORPORATE SOURCE: Department of Microbiology and Immunology, University of Michigan, Ann Arbor, MI, 48109-0666, USA
SOURCE: Journal of Biological Chemistry (2001), 276(21), 17920-17931
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Dendritic cells (DCs) are antigen-presenting cells that play a major role in initiating primary immune responses. The authors have utilized two independent approaches, DNA microarrays and proteomics, to analyze the expression profile of human CD14+ blood monocytes and their derived DCs. Anal. of gene expression changes at the RNA level using oligonucleotide microarrays complementary to 6300 human genes showed that .apprx.40% of the genes were expressed in DCs. A total of 255 genes (4%) were regulated during DC differentiation or maturation. Most of these genes were not previously associated with DCs and included genes encoding secreted proteins as well as genes involved in cell adhesion, signaling, and lipid metabolism Protein anal. of the same cell populations was done using two-dimensional gel electrophoresis. A total of 900 distinct protein spots were included, and 4% of them exhibited quant. changes during DC differentiation and maturation. Differentially expressed proteins were identified by mass spectrometry and found to represent proteins with Ca2+ binding, fatty acid binding, or chaperone activities as well as proteins involved in cell motility. In addition, proteomic anal. provided an assessment of post-translational modifications. The chaperone protein, calreticulin, was found to undergo cleavage, yielding a novel form. The combined oligonucleotide microarray and proteomic approaches have uncovered novel genes associated with DC differentiation and maturation and has allowed anal. of post-translational modifications of specific proteins as part of these processes.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 14 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:790660 CAPLUS
DOCUMENT NUMBER: 133:349121
TITLE: Methods for increasing T cell proliferation
INVENTOR(S): Van, Den Eynde Benoit; Bilsborough, Janine; Boon-Falleur, Thierry
PATENT ASSIGNEE(S): Ludwig Institute for Cancer Research, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000066764 | A1 | 20001109 | WO 2000-US12118 | 20000503 <-- |
| W: AU, JP | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| EP 1185687 | A1 | 20020313 | EP 2000-928796 | 20000503 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |

PRIORITY APPLN. INFO.: US 1999-132219P P 19990503
WO 2000-US12118 W 20000503

AB The invention provides methods and compns. for increasing T cell proliferation using tryptophan enhancing agents. T cell proliferation can be increased in vitro by addition of tryptophan enhancing agents to T cell culture, or in vivo by administration of tryptophan enhancing agents. Also provided are methods for diagnosing and treating disorders characterized by constitutive expression of indoleamine -2,3-dioxygenase. Compns. and apparatus relating to the methods also are provided.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:670740 CAPLUS
DOCUMENT NUMBER: 134:157226
TITLE: Parallel decrease in neurotoxin quinolinic acid and soluble tumor necrosis factor receptor p75 in serum during highly active antiretroviral therapy of HIV type 1 disease
AUTHOR(S): Look, Markus P.; Altfeld, Markus; Kreuzer, Karl A.; Riezler, Rainer; Stabler, Sally P.; Allen, Robert H.; Sauerbruch, Tilman; Rockstroh, Jurgen K.
CORPORATE SOURCE: Department of General Internal Medicine, University of Bonn, Bonn, 53105, Germany
SOURCE: AIDS Research and Human Retroviruses (2000), 16(13), 1215-1221
CODEN: ARHRE7; ISSN: 0889-2229
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chronic immune activation state in HIV disease leads to increased activity of the rate-limiting tryptophan-kynurenine pathway enzyme indoleamine 2,3-dioxygenase (2,3-IDO), thereby increasing the formation of neurotoxic tryptophan metabolites such as kynurenine and quinolinic acid. We investigated whether highly active

antiretroviral therapy (HAART) (median duration, 100 days; range, 50-188 days) lowers serum levels of these metabolites in HIV-infected individuals and if so, whether this was paralleled by changes in a surrogate marker for immune activation, i.e., soluble tumor necrosis factor receptor p75 (sTNFR p75) concns. Baseline quinolinic acid (848 nM, 95% CI 567-1130 vs. 303 nM, 95% CI 267.1-339.5) and kynurenine (4.1 μM, 95% CI 3.3-4.9 vs. 2.7 μM, 95% CI 2.4-2.9) concns. as well as the mean kynurenine-to-tryptophan ratio (108.2, 95% CI 76.1-140.4 vs. 51.4, 95% CI 47.6-55.3) in 17 HIV-1-infected outpatients (7 with AIDS) were significantly higher than those in 55 healthy age-matched controls ($p < 0.01$), resp. Serum quinolinic acid concns. in 14 of 17 patients decreased (mean, -44.4%) during HAART in comparison with baseline (471.2 nM, 95% CI 288-654.3; $p = 0.022$). Thirteen of these 14 patients also had decreases in sTNFR p75 concns. Overall, the mean sTNFR p75 concentration decreased by 36.3% (13.5 ng/mL, 95% CI 9.3-17.8 vs. 8.6 ng/mL, 95% CI 5.9-11.4; $p = 0.01$, $n = 17$). Reduction in viral load through HAART and subsequent mitigation of the pathol. immune activation state in HIV disease may have reduced 2,3-IDO over activation. This eventually led to a decrease in quinolinic acid formation. The parallel reduction of the immune activation marker sTNFR p75 supports this hypothesis.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:615616 CAPLUS

DOCUMENT NUMBER: 134:188864

TITLE: Maturation of Human Monocyte-Derived Dendritic Cells Studied by Microarray Hybridization

AUTHOR(S): Dietz, Allan B.; Bulur, Peggy A.; Knutson, Gaylord J.; Matasic, Richard; Vuk-Pavlovic, Stanimir

CORPORATE SOURCE: Stem Cell Laboratory, Mayo Clinic Cancer Center, Mayo Clinic, Rochester, MN, 55905, USA

SOURCE: Biochemical and Biophysical Research Communications ( 2000), 275(3), 731-738
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We compared the transcript profiles of human myeloid immature dendritic (IDC) cells and mature dendritic cells (MDC) by hybridization of cell-derived cDNA to DNA probes immobilized on microarrays. The microarrays contained probes for 4110 known genes. We report maturation-dependent changes in transcription of clusters of differentiation, cytokines, cytokine receptors, chemokines, chemokine receptors, neuropeptides, adhesion mols., and other genes. We identified 1124 transcripts expressed in IDC and 1556 transcripts expressed in MDC. Maturation increased the levels of 291 transcripts twofold or more and reduced the levels of 78 transcripts to one-half or less than in IDC. We identified a concerted maturation-stage-dependent transcription of the variable chains of the members of the γ-chain-cytokine receptor family IL-4R, IL-7R, and IL-15R. Also, we found the reversal of the ratio of transcripts for galectin-3 and galectin-9 upon maturation. We identified maturation-dependent changes in the levels of transcripts for numerous genes encoding proteins previously undetected in dendritic cells such as indoleamine 2,3-deoxygenase, Epstein-Barr virus induced protein 3 and kinesin-2. Moreover, MDC transcribed and translated insulin like growth factor-1 receptor, transforming growth factor α, and neuropeptide Y. Full exptl. details are described in the electronic version of this paper available at http://www.mayo.edu/research/vuk_lab/. 

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:403419 CAPLUS
DOCUMENT NUMBER: 133:129960
TITLE: Melatonin, experimental basis for a possible application in breast cancer prevention and treatment
AUTHOR(S): Cos, S.; Sanchez-Barcelo, E. J.
CORPORATE SOURCE: Department of Physiology and Pharmacology, University of Cantabria, Santander, 39011, Spain
SOURCE: Histology and Histopathology (2000), 15(2), 637-647
CODEN: HIHIES; ISSN: 0213-3911
PUBLISHER: Histology and Histopathology
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with .apprx.120 refs. The role of the pineal as an oncostatic gland has been studied in animal models of tumorigenesis, especially on those concerning the mammary gland. The general conclusion is that exptl. manipulations activating pineal gland, or the administration of melatonin, reduce the incidence and growth rate of chemical-induced murine mammary tumors, while pinealectomy or situations which implicate a reduction of melatonin production usually stimulate mammary carcinogenesis. The direct actions of melatonin on mammary tumors have been suggested because of its ability to inhibit, at physiol. doses (1nM), the in vitro proliferation of MCF-7 human breast cancer cells. In this article we review the outstanding findings related to melatonin actions on mammary which, taken together, support a possible usefulness of this indoleamine in the prevention and treatment of mammary gland malignancy.
REFERENCE COUNT: 105 THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2000:152116 CAPLUS
DOCUMENT NUMBER: 133:53257
TITLE: Inhibition of tumor growth by L-deprenyl involves neural-immune interactions in rats with spontaneously developing mammary tumors
AUTHOR(S): Thyagarajan, Srinivasan; Madden, Kelley S.; Stevens, Suzanne Y.; Felten, David L.
CORPORATE SOURCE: Center for Neuroimmunology, Loma Linda University School of Medicine, Loma Linda, CA, 92350, USA
SOURCE: Anticancer Research (1999), 19(6B), 5023-5028
CODEN: ANTRD4; ISSN: 0250-7005
PUBLISHER: International Institute of Anticancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English
AB L-deprenyl, a monoamine oxidase-B inhibitor, has been shown to reverse the age-related decline in sympathetic noradrenergic innervation and immune function in old rats and enhance T cell and NK cell activity in tumor-bearing rats. The objective of the present study was to examine whether deprenyl treatment of old female rats with mammary tumors could augment sympathetic nervous system and immune responses to inhibit the tumor growth. Female Sprague-Dawley rats with spontaneous mammary tumors were administered 0, 2.5 mg, or 5.0 mg/kg body weight (BW)/day deprenyl for i.p. 9 wk. Tumor diameter, tumor number and body weight were measured throughout the treatment period. At the end of the treatment period, norepinephrine (NE) concentration, interferon-γ production (IFN-γ), Con A-induced T

lymphocyte proliferation, and percentage of T and B lymphocytes and natural killer cells were measured in the spleen, and the concns. of monoamines were measured in the medial basal hypothalamus. Relative to saline-treated controls, treatment with deprenyl reduced tumor growth, increased NE concentration, IFN-γ production and percentage of the CD8+ T lymphocytes in the spleen. In the medial basal hypothalamus, deprenyl treatment increased the concns. of catecholamines and indoleamine . These results suggest that the anti-tumor effects of deprenyl on spontaneous rat mammary tumors may be achieved via neural-immune signaling in the spleen and medial basal hypothalamus.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 19 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2000:145067 CAPLUS
DOCUMENT NUMBER: 132:206569
TITLE: Expression monitoring for human cytomegalovirus (HCMV) infection, and genes possibly involved in mediating the pathology of HCMV infection
INVENTOR(S): Zhu, Hua; Gingeras, Thomas; Shenk, Thomas
PATENT ASSIGNEE(S): Affymetrix, Inc., USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000011218 | A1 | 20000302 | WO 1999-US18772 | 19990820 <-- |
| WO 2000011218 | A9 | 20020829 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9956776 | A1 | 20000314 | AU 1999-56776 | 19990820 <-- |
| PRIORITY APPLN. INFO.: | | | US 1998-97708P P | 19980821 |
| | | | WO 1999-US18772 W | 19990820 |

AB The invention provides methods, compns., and apparatus for studying the complex regulatory relationships among host genes and viruses, in particular HCMV. The invention also provides cellular mRNAs whose levels change by a factor of four or more after infection with HCMV. Such genes are likely those involved in mediating the pathol. of the infected tissues. Thus by identifying agents which are able to reverse the induction or repression of such genes, one can find candidate therapeutic agents for use in treating and or preventing HCMV-caused disease pathologies.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1999:527609 CAPLUS
DOCUMENT NUMBER: 131:266696
TITLE: L-Deprenyl inhibits tumor growth, reduces serum prolactin, and suppresses brain monoamine metabolism in rats with carcinogen-induced mammary tumors

AUTHOR(S): ThyagaRajan, Srinivasan; Quadri, S. Kaleem
CORPORATE SOURCE: Neuroendocrine Research Laboratory, Kansas State University, Manhattan, KS, USA
SOURCE: Endocrine (1999), 10(3), 225-232
CODEN: EOCRE5; ISSN: 1355-008X
PUBLISHER: Humana Press Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previously, we have reported that L-deprenyl decreased the incidence of mammary tumors and pituitary tumors in old acyclic rats. The objective of the present study was to investigate the effects of L-deprenyl, a monoamine oxidase-B (MAO-B) inhibitor, treatment on the development and growth of tumors and on the metabolism of catecholamines and indoleamine in the medial basal hypothalamus (MBH) and the striatum (ST) of rats bearing 7, 12-dimethylbenzanthracene (DMBA)-induced mammary tumors. Female Sprague-Dawley rats with DMBA-induced mammary tumors were injected (s.c.) daily with 0.25 mg or 5.0 mg of deprenyl/kg BW or the vehicle (saline; control) for 12 wk. Tumor diameter, tumor number, body weight, and feed intake were measured every week of the treatment period. Serum PRL and the concns. of catecholamines, indoleamine , and their metabolites were measured by RIA and HPLC, resp. Treatment with 5.0 mg deprenyl decreased the tumor diameter, tumor number, and serum prolactin (PRL) level. Although the body weight increased in all three groups, the body weight gain in the 5.0 mg group was smaller than that in the control and 0.25 mg groups. Deprenyl treatment had no effect on feed intake. The concns. of dihydroxyphenylacetic acid (DOPAC) and homovanillic acid (HVA) were decreased in the MBH and the ST, and the concentration of 5-hydroxyindoleacetic acid (5-HIAA) was decreased in the MBH of deprenyl-treated rats. Treatment with 5.0 mg deprenyl enhanced the concns. of norepinephrine (NE) and serotonin (5-HT) in the MBH and in the ST, and the concentration of dopamine (DA) in the MBH. These results suggest that the suppression of the development and growth of DMBA-induced mammary tumors by chronic deprenyl treatment may be mediated through alterations in the synthesis and metabolism of catecholamines and indoleamine in the MBH and inhibition of PRL secretion.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1999:388082 CAPLUS
DOCUMENT NUMBER: 131:35866
TITLE: Regulation of T cell-mediated immunity by tryptophan
INVENTOR(S): Munn, David; Mellor, Andrew
PATENT ASSIGNEE(S): Medical College of Georgia Research Institute, Inc., USA
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9929310 | A2 | 19990617 | WO 1998-US25840 | 19981204 <-- |
| WO 9929310 | A3 | 20000106 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,

UA, UG, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| AU 9916285 | A | 19990628 | AU 1999-16285 | 19981204 <-- |
| US 6395876 | B1 | 20020528 | US 1998-205939 | 19981204 <-- |
| US 6451840 | B1 | 20020917 | US 1998-206274 | 19981204 <-- |
| US 2001001040 | A1 | 20010510 | US 2000-727055 | 20001130 <-- |
| US 6482416 | B2 | 20021119 | | |
| US 2002155104 | A1 | 20021024 | US 2002-112362 | 20020328 <-- |
| US 7160539 | B2 | 20070109 | | |
| US 2007077224 | A1 | 20070405 | US 2006-602930 | 20061121 |
| US 2007077234 | A1 | 20070405 | US 2006-603291 | 20061121 |

PRIORITY APPLN. INFO.:

| | | |
|---|---|---|
| US 1997-67610P | P | 19971205 |
| US 1998-80380P | P | 19980401 |
| US 1998-80384P | P | 19980401 |
| US 1998-206274 | A3 | 19981204 |
| WO 1998-US25840 | W | 19981204 |
| US 2002-112362 | A3 | 20020328 |

AB A mechanism of macrophage-induced T cell suppression is the selective elimination of tryptophan and/or increase in one or more tryptophan metabolites within the local macrophage microenvironment. Studies demonstrate that expression of IDO (indoleamine 2,3-dioxygenase) can serve as a marker of suppression of T cell activation, and may play a significant role in allogeneic pregnancy and therefore other types of transplantation, and that inhibitors of IDO can be used to activate T cells and therefore enhance T cell activation when the T cells are suppressed by pregnancy, malignancy or a virus such as HIV. Inhibiting tryptophan degradation (and thereby increasing tryptophan concentration while decreasing tryptophan metabolite concentration), or supplementing tryptophan concentration, can therefore be used in addition to, or in place of, inhibitors of IDO. Similarly, increasing tryptophan degradation (thereby, decreasing tryptophan concentration and increasing tryptophan metabolite concentration), for example, by increasing IDO concentration or IDO activity, can suppress T cells. Although described particularly with reference to IDO regulation, one can instead manipulate local tryptophan concns., and/or modulate the activity of the high affinity tryptophan transporter, and/or administer other tryptophan degrading enzymes. Regulation can be further manipulated using cytokines such as macrophage colony stimulating factor, interferon gamma, alone or in combination with antigen or other cytokines.

L3 ANSWER 22 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

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|---|---|
| ACCESSION NUMBER: | 1998:765634 CAPLUS |
| DOCUMENT NUMBER: | 130:137555 |
| TITLE: | Cellular gene expression altered by human cytomegalovirus: global monitoring with oligonucleotide arrays |
| AUTHOR(S): | Zhu, Hua; Cong, Jian-Ping; Mamtora, Gargi; Gingeras, Thomas; Shenk, Thomas |
| CORPORATE SOURCE: | Howard Hughes Medical Institute, Department of Molecular Biology, Princeton University, Princeton, NJ, 08544, USA |
| SOURCE: | Proceedings of the National Academy of Sciences of the United States of America (1998), 95(24), 14470-14475<br>CODEN: PNASA6; ISSN: 0027-8424 |
| PUBLISHER: | National Academy of Sciences |
| DOCUMENT TYPE: | Journal |

LANGUAGE: English

AB Mechanistic insights to viral replication and pathogenesis generally have come from the anal. of viral gene products, either by studying their biochem. activities and interactions individually or by creating mutant viruses and analyzing their phenotype. Now it is possible to identify and catalog the host cell genes whose mRNA levels change in response to a pathogen. We have used DNA array technol. to monitor the level of ≈6,600 human mRNAs in uninfected as compared with human cytomegalovirus-infected cells. The level of 258 mRNAs changed by a factor of 4 or more before the onset of viral DNA replication. Several of these mRNAs encode gene products that might play key roles in virus-induced pathogenesis, identifying them as intriguing targets for further study.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:649638 CAPLUS

DOCUMENT NUMBER: 130:2998

TITLE: Effect of cytokines on growth of Toxoplasma gondii in murine astrocytes

AUTHOR(S): Halone, S. K.; Chiu, F.-C.; Weiss, L. M.

CORPORATE SOURCE: Department of Neurology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA

SOURCE: Infection and Immunity (1998), 66(10), 4989-4993
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cytokines play a role in the regulation of T. gondii in the central nervous system. Cytokine-activated microglia are important host defense cells in central nervous system infections. Recent evidence indicates that astrocytes can also be activated by cytokines to inhibit intracellular pathogens. Here, the authors examined the effect of γ interferon (IFN-γ), tumor necrosis factor α (TNF-α), interleukin-6 (IL-6), and IL-1 on the growth of T. gondii in a primary murine astrocyte culture. Pretreatment of astrocytes with IFN-γ resulted in 65% inhibition of T. gondii growth. Neither TNF-α, IL-1, nor IL-6 alone had any effect on T. gondii growth. IFN-γ in combination with either TNF-α, IL-1, or IL-6 caused a 75-80% inhibition of growth. While nitric oxide was produced by astrocytes treated with these cytokines, inhibition of T. gondii growth was not reversed by the addition of the nitric oxide synthase inhibitor NG-monomethyl-L-arginine. Furthermore, IFN-γ in combination with IL-1, IL-6, or TNF-α also induced inhibition in astrocytes derived from syngeneic mice deficient in the enzyme inducible nitric oxide synthase. Apparently, the mechanism of cytokine inhibition is not nitric oxide mediated. Similarly, the addition of tryptophan had no effect on inhibition, indicating that the mechanism was not mediated via induction of the enzyme indoleamine 2,3-dioxygenase. The mechanism of inhibition remains to be elucidated. These results demonstrate that cytokine-activated astrocytes are capable of inhibiting the growth of T. gondii. Astrocytes may thus be important host defense cells in controlling toxoplasmosis in the brain.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:191552 CAPLUS

DOCUMENT NUMBER: 128:290477

TITLE: Melatonin enhances tamoxifen's ability to prevent the

reduction in microsomal membrane fluidity induced by lipid peroxidation
AUTHOR(S): Garcia, J. J.; Reiter, R. J.; Ortiz, G. G.; Oh, C. S.; Tang, L.; Yu, B. P.; Escames, G.
CORPORATE SOURCE: Department of Cellular and Structural Biology, University of Texas Health Science Center, San Antonio, TX, 78284, USA
SOURCE: Journal of Membrane Biology (1998), 162(1), 59-65
CODEN: JMBBBO; ISSN: 0022-2631
PUBLISHER: Springer-Verlag New York Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The indoleamine melatonin and the synthetic antiestrogenic drug tamoxifen seem to have similar mechanisms in inhibiting the growth of estrogen receptor pos. breast cancer cells. In this study, the authors compared the ability of these mols., alone and in combination, in stabilizing microsomal membranes against free radical attack. Hepatic microsomes were obtained from male rats and incubated with or without tamoxifen (50-200 FM), melatonin (1 mM) or both; lipid peroxidn. was induced by addition of FeCI3, NADPH and ADP. After oxidative damage, membrane fluidity, measured by fluorescence polarization techniques, decreased, whereas malonaldehyde (MDA) and 4-hydroxyalkenals (4-HDA) concns. increased. Incubation of the microsomes with tamoxifen prior to exposure to free radical generating processes inhibited, in a dose-dependent manner, the increase in membrane rigidity and the rise in MDA+4-HDA levels. When melatonin was added, the efficacy of tamoxifen in preventing membrane rigidity was enhanced. Thus, the IC50s for preventing membrane rigidity and for inhibiting lipid peroxidn. obtained for tamoxifen in the presence of melatonin were lower than those obtained with tamoxifen alone. Moreover, tamoxifen (50-200 μM) in the presence of melatonin reduced basal membrane fluidity and MDA+4-HDA levels in microsomes. These synergistic effects of tamoxifen and melatonin in stabilizing biol. membranes may be important in protecting membranes from free radical damage.
REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:72933 CAPLUS
DOCUMENT NUMBER: 128:225774
TITLE: Antitumor effect of l-deprenyl in rats with carcinogen-induced mammary tumors
AUTHOR(S): ThyagaRajan, Srinivasan; Felten, Suzanne Y.; Felten, David L.
CORPORATE SOURCE: Department of Neurobiology and Anatomy, University of Rochester School of Medicine, Rochester, USA
SOURCE: Cancer Letters (Shannon, Ireland) (1998), 123(2), 177-183
CODEN: CALEDQ; ISSN: 0304-3835
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Deprenyl, a monoamine oxidase-B (MAO-B) inhibitor, has a wide range of pharmacol. properties that are beneficial therapeutically in the treatment of human neurodegenerative diseases. Recent studies have demonstrated that deprenyl possesses a neuroprotective function that is not dependent on its MAO-B inhibitory activity. The focus of the present study was to investigate whether prolonged treatment of young Sprague-Dawley female rats with deprenyl before and after 9,10-dimethyl-1,2-benzanthracene (DMBA) administration would inhibit the development of mammary tumors by exerting a neuroprotective

effect on the tuberoinfundibular dopaminergic (TIDA) neurons in the medial basal hypothalamus (MBH). For this purpose, the concns. of catecholamines, indoleamine and their metabolites were measured in the MBH by high-performance liquid chromatog. (HPLC) at the end of the treatment period. Female Sprague-Dawley rats (28-29 days old) were treated i.p. with saline, or 0.25 or 2.5 mg of deprenyl/kg b.w. daily for 4 wk prior to the administration of DMBA. Following the administration of DMBA, the rats were treated with saline or deprenyl daily for 27 wk. At the end of the treatment period, there was a significant reduction in the tumor incidence and tumor number in rats that received 2.5 mg/kg deprenyl before and after the administration of DMBA and also in rats that were treated with 2.5 mg/kg deprenyl following DMBA. There also was a significant decrease in tumor number in rats that were treated with 0.25 mg/kg deprenyl during the entire treatment period of 31 wk. Body weight increased throughout the treatment period with no significant differences between the groups. Treatment of rats with 2.5 mg of deprenyl following the administration of DMBA and also during the entire treatment period resulted in a significant decrease in the concns. of the metabolites of norepinephrine (NE), dopamine (DA) and serotonin (5-HT) in the MBH, but there were no significant alterations in the concns. of NE, DA and 5-HT in the MBH. These results suggest that the administration of deprenyl blocked the development of mammary tumors in part by inhibiting the metabolism of catecholamines and indoleamine and possibly by conferring a neuroprotective effect on the TIDA neurons in the MBH, especially at 0.25 mg/kg of deprenyl.

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 26 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1998:35862 CAPLUS

DOCUMENT NUMBER: 128:139599

TITLE: Multiple molecular and cellular changes associated with tumor stasis and regression during IL-12 therapy of a murine breast cancer model

AUTHOR(S): Dias, Sergio; Thomas, Hilary; Balkwill, Frances

CORPORATE SOURCE: Biological Therapies Laboratory, Imperial Cancer Research Fund, London, WC2A 3PX, UK

SOURCE: International Journal of Cancer (1998), 75(1), 151-157
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB IL-12 treatment of a murine transplantable breast carcinoma (HTH-K) led to tumor regression and cure which was related to the duration of treatment. The authors studied the sequential mol. and phenotypic changes in IL-12-treated tumors. IFN-γ mRNA was detected 8 h after the first treatment. MRNA expression for the IFN-γ-inducible genes β2-microglobulin and indoleamine dioxygenase ( IDO) was induced subsequently, together with the chemokine IP-10. IL-12-treated tumors had an abundant cellular infiltrate, consisting mainly of CD8+ T cells. MRNA for granzyme B and perforin also could be detected, suggesting that those cells were activated. After 7 days of daily therapy, tumors in IL-12-treated mice had a reduction in vasculature. Finally, the number of apoptotic tumor cells increased throughout IL-12 treatment. The authors compared the antitumor effects of IL-12 to those induced by IFN-γ therapy, which caused initial tumor stasis but subsequent tumor progression. IFN-γ induced β2-microglobulin and IDO over a 7-day period, but IP-10 was induced only transiently. IFN-γ caused a lesser cellular infiltrate, a minor anti-angiogenic effect, and a

transient apoptotic effect. The success of IL-12 may be due to its ability to produce a distinct sequence of mol. and phenotypic changes in tumors, leading to an antitumor immune response, toxicity against tumor cells, and an anti-angiogenic effect. Other cytokines, such as IFN-γ, induce some, but not all, of these actions. Comparison of IL-12 and IFN-γ suggests that sustained induction of IP-10 and activation of a resulting cellular infiltrate may be key changes in regressing tumors.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 27 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:694251 CAPLUS
DOCUMENT NUMBER: 125:326402
TITLE: An immunoreactive conjugate, method for its preparation, antibodies to the conjugate and a pharmaceutical composition and diagnostic device containing them
INVENTOR(S): Maes, Roland
PATENT ASSIGNEE(S): Anda Biologicals S.A., Fr.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | | DATE |
|---|---|---|---|---|---|
| EP 736770 | A2 | 19961009 | EP 1996-870042 | | 19960401 <-- |
| EP 736770 | A3 | 19970502 | | | |
| R: BE, DE, FR, GB, IT | | | | | |
| BE 1009230 | A6 | 19970107 | BE 1995-316 | | 19950405 <-- |
| BE 1009917 | A6 | 19971104 | BE 1996-113 | | 19960208 <-- |
| PRIORITY APPLN. INFO.: | | | BE 1995-316 | A | 19950405 |
| | | | BE 1996-113 | A | 19960208 |

AB An immunoreactive conjugate is disclosed which contains 1 or more haptens consisting of a sulfhydryl group and one of the following: amino acids, carbohydrates, amino carbohydrates, phosphatidylinositol, sphingosine, and their nitrosyl, acyl, or acetyl derivs., the haptens being coupled to a protein with a mol. weight >8000 Kd and/or a solid support by a coupling agent capable of binding to the sulfhydryl group of the hapten. Thus, NO-cysteine and NO-N-acetyl-L-cysteine conjugates with albumin were prepared, and birds and mammals were vaccinated. IgG and IgM class antibodies specific for N-acetyl-L-cysteine were detected in the subjects. Addnl. analyses demonstrated that many HIV-pos. patients have IgG specific for acetyl-cysteine. Pharmaceutical compns. using these immunoreactive conjugates can be used in the prevention and/or treatment of autoimmunity, AIDS, cancer, tuberculosis and a variety of other diseases.

L3 ANSWER 28 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1996:402922 CAPLUS
DOCUMENT NUMBER: 125:84214
TITLE: Molecular mechanisms underlying IFN-γ-mediated tumor growth inhibition induced during tumor immunotherapy with rIL-12
AUTHOR(S): Yu, Wen-Gong; Yamamoto, Norihiko; Takenaka, Hiroshi; Mu, Jie; Tai, Xu-Guang; Zou, Jian-Ping; Ogawa, Makoto; Tsutsui, Taeki; Wijesuriya, Rishani; et al.
CORPORATE SOURCE: Biomed. Res. Cent., Osaka Univ., Suita, 565, Japan
SOURCE: International Immunology (1996), 8(6), 855-865

CODEN: INIMEN; ISSN: 0953-8178
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigates the mol. mechanisms by which IFN-γ produced as a result of in vivo IL-12 administration exerts its anti-tumor effects. RIL-12 was administered 3 or 5 times into mice bearing CSA1M fibrosarcoma, OV-HM ovarian carcinoma, or MCH-1-A1 fibrosarcoma. This regimen induced complete regression of CSA1M and OV-HM tumors but only transient growth inhibition of MCH-1-A1 tumors. The anti-tumor effects of IL-12 were associated with enhanced induction of IFN-γ because these effects were abrogated by pretreatment of hosts with anti-IFN-γ antibody. Exposure in vitro of the 3 types of tumor cells to rIFN-γ resulted in moderate to potent inhibition of tumor cell growth. IFN-γ stimulated the expression of mRNAs for an inducible type of NO synthase (iNOS) in CSA1M cells and indoleamine 2,3-dioxygenase ( IDO), an enzyme capable of degrading tryptophan, in OV-HM cells, but induced only marginal levels of these mRNAs in MCH-1-A1 cells. In association with iNOS gene expression, IFN-γ-stimulated CSA1M cells produced a large amount of NO which functioned to inhibit their own growth in vitro. Although OV-HM and MCH-1-A1 cells did not produce NO, they also exhibited NO susceptibility. Whereas the tumor masses from IL-12-treated CSA1M-bearing or OV-HM-bearing mice induced higher levels of iNOS (for CSA1M) or IDO and iNOS (for OV-HM) mRNAs, the MCH-1-A1 tumor mass expressed lower levels of iNOS mRNA alone. Moreover, massive infiltration of CD4+ and CD8+ T cells and Mac-1+ cells was seen only in the CSA1M and OV-HM tumors. Thus, IFN-γ produced after IL-12 treatment induces the expression of various genes with potential to modulate tumor cell growth by acting directly on tumor cells or stimulating tumor-infiltrating lymphoid cells and the effectiveness of IL-12 therapy is associated with the operation of these mechanisms.

L3 ANSWER 29 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1995:368434 CAPLUS
DOCUMENT NUMBER: 122:158241
TITLE: The role of indoleamine 2,3-dioxygenase in the anti-tumor activity of human interferon-γ in vivo
AUTHOR(S): Burke, Frances; Knowles, Richard G.; East, Nick; Balkwill, Frances R.
CORPORATE SOURCE: Biological Therapy Laboratory, Imperial Cancer Research Fund, London, WC2A 3PX, UK
SOURCE: International Journal of Cancer (1995), 60(1), 115-22
CODEN: IJCNAW; ISSN: 0020-7136
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors studied the relation between L-tryptophan metabolism and the response to human IFN-γ in 3 human ovarian cancer xenografts growing in nude mice. During IFN-γ therapy all 3 tumors showed a profound depletion in L-tryptophan and a corresponding rise in L-kynurenine. The microenvironment surrounding the tumors was also depleted of L-tryptophan. The IFN-γ-inducible enzyme indoleamine dioxygenase, IDO, was induced in treated tumors. While there was a variability in IDO mRNA expression in the different xenografts tested, in situ hybridization showed that the gene was induced at all levels of the tumor, and not just the periphery. Thus, induction of IDO by IFN-γ in vivo can metabolize L-tryptophan rapidly enough for it to become depleted, despite a continued

supply of L-tryptophan from the host. The IDO mRNA and protein remained induced after the L-tryptophan levels had returned to normal, suggesting that the gene may be post-transcriptionally regulated and/or the IDO co-factor supply may be limited. Another IFN-γ-inducible gene, tryptophanyl tRNA synthetase, was also induced in the tumor. It is possible that this enzyme, which is responsible for synthesizing tryptophanyl tRNA, acts in a compensatory manner by allowing protein synthesis to continue despite low free L-tryptophan concns. There was no correlation of the above parameters with the antitumor response to IFN-γ, suggesting that other mechanisms must play a role. L-Tryptophan depletion may be a contributor to a multifactorial growth inhibition of tumor cells following IFN-γ treatment, but cannot on its own explain their growth inhibition.

L3 ANSWER 30 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:647695 CAPLUS
DOCUMENT NUMBER: 119:247695
TITLE: Reversal of an interferon-γ-resistant phenotype by poly(I:C): Possible role of double-stranded RNA-activated kinase in interferon-γ signaling
AUTHOR(S): Ozes, Osman N.; Taylor, Milton W.
CORPORATE SOURCE: Dep. Biol., Indiana Univ., Bloomington, IN, 47405, USA
SOURCE: Journal of Interferon Research (1993), 13(4), 283-8
CODEN: JIREDJ; ISSN: 0197-8357
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO) is induced in neoplastic cell lines by interferon-γ (IFN-γ) treatment. In ME180 cervical carcinoma cells, there is a rapid increase in IDO mRNA accumulation beginning at 4 h after IFN-γ treatment and continuing for at least 24 h. The IFN-γ-resistant mutant of ME180, IR3B6B, expresses very low levels of IDO message after IFN-γ treatment. However, pretreatment of this mutant with poly(I:C) restores normal levels of IDO mRNAs and IDO enzyme activity. Poly(I:C) mediated reversal of the IFN-γ-resistant phenotype and induction of IDO mRNA are inhibited by 2-aminopurine. In vitro phosphorylation of calf thymus histone using the immunopptd. p68 kinase prepared from IFN-γ-treated ME180 and IR3B6B cells revealed the deficiency of activation of this kinase in IR3B6B cells after IFN-γ treatment, and treatment of this mutant cells with poly(I:C) restores p68 kinase activity. From these results, the authors conclude that a double-stranded RNA-dependent kinase is activated by IFN-γ treatment and its activation correlates with IFN-γ-mediated induction of the IDO gene.

L3 ANSWER 31 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:623991 CAPLUS
DOCUMENT NUMBER: 119:223991
TITLE: Induction of pterin synthesis is not required for cytokine-stimulated tryptophan metabolism
AUTHOR(S): Sakai, Naoki; Saito, Kuniaki; Kaufman, Seymour; Heyes, Melvyn P.; Milstien, Sheldon
CORPORATE SOURCE: Lab. Neurochem., Natl. Inst. Ment. Health, Bethesda, MD, 20892, USA
SOURCE: Biochemical Journal (1993), 295(2), 543-7
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Activation of the immune system which occurs in inflammatory diseases leads to parallel increases in pterin synthesis and increased production of

neuroactive L-tryptophan metabolites. Several model systems were studied to determine whether pterins, which are cofactors for hydroxylation reactions, could be required in the oxidative kynurenine pathway of L-tryptophan degradation Treatment of mice with interferon-γ increased L- tryptophan metabolism without any corresponding change in tissue biopterin concns. Cytokine-treated human fibroblasts, macrophages and glioblastoma cells all showed increases in kynurenine production, which were completely independent of pterin synthesis. When pterin synthesis de novo was blocked, either by an inhibitor of GTP cyclohydrolase or because of a genetic deficiency of one of the enzymes of the pathway of pterin biosynthesis, cytokine-stimulated increases in tryptophan metabolism were unaffected. Furthermore, increasing intracellular tetrahydrobiopterin concns. by treating cells with sepiapterin also had no effect on markers of tryptophan metabolism Therefore, both normal and cytokine-stimulated L-tryptophan metabolism appears to be completely independent of pterin biosynthesis.

L3 ANSWER 32 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:426374 CAPLUS
DOCUMENT NUMBER: 119:26374
TITLE: Induction of toxoplasmostasis in a human glioblastoma by interferon γ
AUTHOR(S): Daeubener, Walter; Pilz, Korinna; Zennati, Samira Seghrouchni; Bilzer, Thomas; Fischer, Hans Georg; Hadding, Ulrich
CORPORATE SOURCE: Inst. Med. Mikrobiol. Virol., Heinrich-Heine-Univ., Duesseldorf, D-4000, Germany
SOURCE: Journal of Neuroimmunology (1993), 43(1-2), 31-8
CODEN: JNRIDW; ISSN: 0165-5728
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the course of human toxoplasmosis, central nervous system involvement often occurs. As a model for toxoplasma growth within human brain cells, the proliferation of Toxoplasma gondii strain BK within the human glioblastoma cell line 86HG39 was analyzed. The 86HG39 cells support the growth of toxoplasma similar to human monocyte derived macrophages and in contrast to human monocytes. The growth of T. gondii within interferon γ (IFNγ)-treated 86HG39 cells is reduced due to toxoplasmostasis and not due to toxoplasmocide effects. The mechanism of IFNγ-induced toxoplasmostasis was also investigated. IFNγ did not induce O2- production and/or nitrite oxide production, and inhibitors of O2- and NO2- did not influence IFNγ-induced toxoplasmostasis. In contrast, the supplementation of L-tryptophan to the culture medium completely abolished the IFNγ effect. Apparently, the induction of L-tryptophan degradation in 86HG39 cells by IFNγ, possibly by activation of the indoleamine-2,3-dioxygenase, is responsible for the IFNγ-induced toxoplasmostasis within the glioblastoma cell line.

L3 ANSWER 33 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:232062 CAPLUS
DOCUMENT NUMBER: 118:232062
TITLE: Tryptophan protects human melanoma cells against γ-interferon and tumor necrosis factor-α: a unifying mechanism of action
AUTHOR(S): Wood, J. M.; Ehrke, C.; Schallreuter, K. U.
CORPORATE SOURCE: Gray Freshwater Biol. Inst., Navarre, MN, 55392, USA
SOURCE: Melanoma Research (1991), 1(3), 177-85
CODEN: MREEEH; ISSN: 0960-8931
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The sensitivity and resistance of 6 human melanoma cell lines to

γ-interferon (γ-IFN) and tumor necrosis factor-α (TNF-α) were examined Amelanotic cell lines were more sensitive to γ-IFN and TNF-α than melanotic cells. The cytotoxicity of γ-IFN and TNF-α could be reversed in all cells by the addition of L- or D-tryptophan to the culture medium. Melanoma cells resistant to γ-IFN excrete Ca-activated neutral protease (CANP) and as a consequence, make L-tryptophan available by the hydrolysis of serum proteins in the culture medium. Resistance to γ-IFN could be reversed by the addition of specific CANP inhibitor, whereas γ-IFN-sensitive strains became more resistant with the addition of CANP to the culture medium. It has been confirmed that γ-IFN induces indoleamine 2,3-dioxygenase in melanoma cells. This enzyme utilizes the superoxide anion (O2-) as a substrate for the oxidation of either L- or D-tryptophan to N-formylkynurenine leading to cell death. The induction of this degradative pathway for L-tryptophan kills cells by starvation of this essential and relatively scarce amino acid. TNF-α induces Mn-containing superoxide dismutase (MnSOD) which also uses O2- to produce cytotoxic concns. of H2O2. Therefore, it can be concluded that the cytotoxicity of both γ-IFN and TNF-α depends on the availability of L-tryptophan as the substrate for the removal of O2- via indoleamine 2,3-dioxygenase.

L3 ANSWER 34 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:204906 CAPLUS
DOCUMENT NUMBER: 118:204906
TITLE: 4-Chloro-3-hydroxyanthranilate, 6-chlorotryptophan and norharmane attenuate quinolinic acid formation by interferon-γ-stimulated monocytes (THP-1 cells)
AUTHOR(S): Saito, Kuniaki; Chen, Cai Y.; Masana, Monica; Crowley, Jeffrey S.; Markey, Sanford P.; Heyes, Melvyn P.
CORPORATE SOURCE: Lab. Clin. Sci., Natl. Inst. Mental Health, Bethesda, MD, 20892, USA
SOURCE: Biochemical Journal (1993), 291(1), 11-14
CODEN: BIJOAK; ISSN: 0306-3275
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Accumulation of quinolinic acid and L-kynurenine occurs in the brain and/or blood following immune activation, and may derive from L-tryptophan following induction of indoleamine 2,3-dioxygenase and other kynurenine-pathway enzymes. In the present study a survey of various cell lines derived from either brain or systemic tissues showed that, while all cells examined responded to interferon-γ by increased conversion of L-[13C6]tryptophan into L-kynurenine (human: B-lymphocytes, neuroblastoma, glioblastoma, lung, liver, kidney; rat brain: microglia, astrocytes and oligodendrocytes), only macrophage-derived cells (peripheral-blood mononuclear cells; THP-1, U-937) and certain liver cells (SKHep1) synthesized [13C6]quniolinic acid. Tumor necrosis factor-α enhanced the effects of interferon-γ in THP-1 cells. Norharmane, 6-chloro-DL-tryptophan and 4-chloro-3-hydroxyanthranilate attenuated quinolinic acid formation by THP-1 cells with IC50 values of 51 μM, 58 μM and 0.11 μM resp. Norharmane and 6-chloro-DL-tryptophan attenuated L-kynurenine formation with IC50 values of 43 μM and 51 μM resp., whereas 4-chloro-3-hydroxyanthranilate had no effect on L-kynurenine accumulation. The redns. in L-kynurenine and quinolinic acid formation are consistent with the reports that norharmane is an inhibitor of indoleamine 2,3-dioxygenase, 6-chloro-DL-tryptophan is metabolized through the kynurenine pathway, and 4-chloro-3-hydroxyanthranilate is an inhibitor of 3-hydroxyanthranilate 3,4-dioxygenase. These results suggest that many tissues may contribute to the production of L-kynurenine following indoleamine 2,3-dioxygenase induction and immune activation. Quinolinic acid may be directly synthesized from L-tryptophan in both

macrophages and certain types of liver cells, although uptake of quinolinic acid precursors from blood may contribute to quinolinic acid synthesis in cells that cannot convert L-kynurenine into quinolinic acid.

L3 ANSWER 35 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:649764 CAPLUS
DOCUMENT NUMBER: 117:249764
TITLE: Differential induction of indoleamine -2,3-dioxygenase (IDO) by interferon-γ in human gynecologic cancer cells
AUTHOR(S): Leung, Benjamin S.; Stout, Lawrence E.; Shaskan, Edward G.; Thompson, Randall M.
CORPORATE SOURCE: Clin. Hosp., Univ. Minnesota, Minneapolis, MN, 55455, USA
SOURCE: Cancer Letters (Shannon, Ireland) (1992), 66(1), 77-81
CODEN: CALEDQ; ISSN: 0304-3835
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Induction of IDO by interferon-γ (IFN-γ) is thought to be a mechanism underlying the antineoplastic properties of IFN-γ. Since clin. trials with IFN-γ have yielded variable efficacy in treating cancers of gynecol. origin, the effects of IFN-γ on cell growth and IDO activity in cell lines from 7 gynecol. and 5 breast cancers were tested. At a dose of 250 IU/mL, IFN-γ suppressed cell growth and induced IDO activity in 1 cervical (C41), 1 vulva (A431), 1 breast (HS578T), and 2 ovarian (OVCAR-3, CAOV-3) cancer cell lines. Differing inhibition of cell growth, but with no induction of IDO activity, was found with IFN-γ treatment of the other cell lines.

L3 ANSWER 36 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:421185 CAPLUS
DOCUMENT NUMBER: 117:21185
TITLE: Regulation of T-cell proliferation via a novel 5HT1a receptor
INVENTOR(S): Aune, Thomas Martin
PATENT ASSIGNEE(S): Miles Inc., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 9204015 | A2 | 19920319 | WO 1991-US6176 | 19910904 <-- |
| WO 9204015 | A3 | 19920416 | | |
| W: AU, CA, JP | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE | | | | |
| CA 2090688 | A1 | 19920305 | CA 1991-2090688 | 19910904 <-- |
| CA 2090689 | A1 | 19920305 | CA 1991-2090689 | 19910904 <-- |
| AU 9188482 | A | 19920330 | AU 1991-88482 | 19910904 <-- |
| EP 547172 | A1 | 19930623 | EP 1991-918533 | 19910904 <-- |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| JP 06503816 | T | 19940428 | JP 1991-517820 | 19910904 <-- |

PRIORITY APPLN. INFO.: US 1990-578710 A 19900904
WO 1991-US6176 A 19910904

AB Methods of regulating proliferation or functions of activated T-cells exhibiting a 5HT1a receptor involve introducing a sufficient amount of agonists or antagonists to either increase or decrease T-cell

proliferation. The basis for regulating cell proliferation may be via (1) the 5HT1a receptor, (2) serotonin synthesis inhibition, and/or (3) serotonin stimulation of CD8+ subpopulations of activated T-cells. Methods of treating T-cell-dependent diseases, immune deficient diseases, and neoplastic diseases are also disclosed. The 5HT1a receptors on human Jurkat T-cells were studied; the receptors stimulated phosphatidylinositol turnover and increased intracellular Ca2+ concentration in these cells. Both CD4+ and CD8+ T-cells expressed elevated levels of the receptor. Serotonin slightly inhibited proliferation of T-cells in response to PHA but stimulated proliferation of T-cells in response to pokeweed mitogen by over 3-fold.

L3 ANSWER 37 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:236096 CAPLUS
DOCUMENT NUMBER: 116:236096
TITLE: Preparation of 2,4-dideoxy-4,5,6-triacyl-glycero-ido-octonic acids as immunological adjuvants
INVENTOR(S): Vyplel, Hermann
PATENT ASSIGNEE(S): Sandoz-Patent-G.m.b.H., Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| DE 4028680 | A1 | 19920312 | DE 1990-4028680 | 19900910 <-- |

PRIORITY APPLN. INFO.: DE 1990-4028680 19900910
OTHER SOURCE(S): CASREACT 116:236096; MARPAT 116:236096
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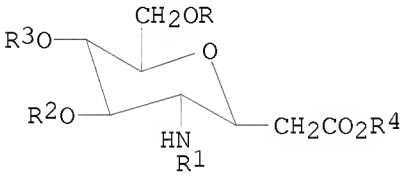


I

AB The title compds. [I; R1-R3 = (un)substituted acyl] (II; R = R4 = H) or their acid salts, useful as immunol. adjuvants having virucidal, antitumor, and antiinflammatory activities, etc.,were prepared by deprotection of their precursors (II; R, R4 = protective group). Thus, 3,7-anhydro-2,4-dideoxy-4-[3-(R)-hydroxytetradecanoylamido]-5,6-di-[3-(R)-hydroxytetradecanoyl]-α-D-glycero-D- ido-octonic acid was prepared by hydrogenation of 3,7-anhydro-4-[3-(R)-benzyloxytetradecanoylamido]-5,6-di-[3-(R)-benzyloxytetradecanoyl]-2,4-dideoxy-8-O-triphenylmethyl-α-D-glycero-D- ido-octonic acid benzyl ester (5-step preparation from 2-[3-(R)-benzyloxytetradecanoylamido]-2-deoxy-4,6-O-isopropylidene-α-D-glucose given) over Pd/C in aqueous THF, followed by stirring of the intermediate deprotected benzyl ester for 48 h with p-MeC6H4SO3H in CHCl3.

L3 ANSWER 38 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:192338 CAPLUS
DOCUMENT NUMBER: 116:192338
TITLE: Analysis of interferon-gamma resistant mutants that are possibly defective in their signal mechanism

AUTHOR(S): Feng, G. S.; Dai, W.; Gupta, S. L.; Werner-Felmayer, G.; Wachter, H.; Takikawa, O.; Taylor, M. W.
CORPORATE SOURCE: Dep. Biol., Indiana Univ., Bloomington, IN, 47405, USA
SOURCE: Molecular and General Genetics (1991), 230(1-2), 91-6
CODEN: MGGEAE; ISSN: 0026-8925
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Previous observations have indicated that mutants partially resistant to IFN-γ cytotoxicity were defective in the induction of indoleamine 2,3-dioxygenase, (IDO). Two mutants highly resistant to IFN-γ were isolated following a second round of mutagenesis. The resistance to IFN-γ was inversely correlated with the inducibility of IDO in these mutants. Moreover, several other IFN-γ responsive genes, including those encoding 2-5A synthetase, GTP cyclohydrolase, and HLA-DRα, were also differentially altered in their expression upon INF-γ treatment. IFN-γ receptor gene expression was not changed nor was the binding of the receptor to IFN-γ. Southern blot anal. failed to reveal any abnormality in the IDO gene structure in these mutants. These mutants may be defective in the IFN-γ signaling pathway and will be useful in further anal. of the biochem. mechanisms of IFN-γ activated gene expression in target cells.

L3 ANSWER 39 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:152268 CAPLUS
DOCUMENT NUMBER: 116:152268
TITLE: Synthesis and biological evaluation of some D-xylofuranosylpyridine C-nucleosides
AUTHOR(S): Verberckmoes, F.; Esmans, E. L.; Dommisse, R. A.; Lepoivre, J. A.; Alderweireldt, F. C.; Balzarini, J.; De Clercq, E.
CORPORATE SOURCE: Lab. Org. Chem., Univ. Antwerp, Antwerp, B-2020, Belg.
SOURCE: Nucleosides & Nucleotides (1991), 10(8), 1771-87
CODEN: NUNUD5; ISSN: 0732-8311
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 116:152268
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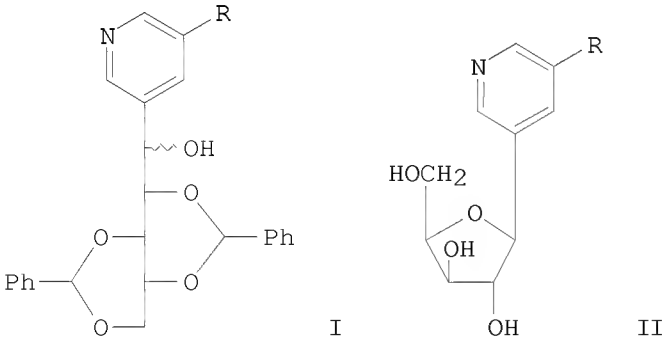


AB The addition reaction of either 3-bromo-5-lithiopyridine or 3-cyano-5-lithiopyridine to 2,4:3,5-di-O-benzylidene-aldehydo-D-xylose gave a D-gulo/D-ido mixture of resp. bromo- and cyano(dibenzylidenepentitolyl)pyridine I (R = Br, cyano). Mesylation of C-1' followed by reaction with CF3CO2H-H2O resulted in the formation of

the corresponding D-xylo-furanosylpyridine C-nucleosides, e.g., II. 3-Cyano-5-D-xylofuranosylpyridine II (R = cyano) was converted to 3-carbamoyl-5-D-xylofuranosylpyridines, e.g., II (R = CONH2), with Amberlite IRA 400 (OH-). The D-xylofuranosyl C-nucleosides were evaluated for their antiviral and cytostatic activity. No significant activity was found.

L3 ANSWER 40 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:104074 CAPLUS
DOCUMENT NUMBER: 116:104074
TITLE: The role of tryptophan and kynurenine transport in the catabolism of tryptophan through indoleamine 2,3-dioxygenase
AUTHOR(S): Knowles, R. G.; Clarkson, N. A.; Pogson, C. I.; Salter, M.; Duch, D. S.; Edelstein, M. P.
CORPORATE SOURCE: Wellcome Res. Lab., Beckenham/Kent, BR3 3BS, UK
SOURCE: Advances in Experimental Medicine and Biology ( 1991), 294(Kynurenine Serotonin Pathways), 161-6
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this report studies were carried out on tryptophan metabolism and transport and on the intracellular concns. of tryptophan and kynurenine in cells in which indoleamine dioxygenase was induced in order to elucidate the role of the plasma membrane transport of tryptophan and kynurenine in the antitumor effects of IFNγ.

L3 ANSWER 41 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:34027 CAPLUS
DOCUMENT NUMBER: 116:34027
TITLE: Immunological effects of levamisole in vitro
AUTHOR(S): Schiller, Joan H.; Lindstrom, Mary; Witt, Patricia L.; Hank, Jacquelyn A.; Mahvi, David; Wagner, Randall J.; Sondel, Paul; Borden, Ernest C.
CORPORATE SOURCE: Dep. Hum. Oncol., William S. Middleton V. A. Hosp., Madison, WI, 53705, USA
SOURCE: Journal of Immunotherapy (1991-1992) (1991), 10(5), 297-306
CODEN: JOIME7; ISSN: 1053-8550
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Levamisole, an antihelminthic drug with immunol. properties, has antitumor activity when administered with 5-fluorouracil in patients with Duke's C colorectal carcinoma. The mechanism of this antitumor effect is unknown, but is postulated to be related to levamisole's immunomodulatory properties. To define further the immunomodulatory activities of levamisole, the authors examined the in vitro effects of levamisole on monocyte and lymphocyte cytotoxicity, activation, and proliferation; induction of cytokine-induced proteins; and expression of tumor -associated antigens. Expts. utilized peripheral blood mononuclear cells from normal donors incubated in the presence of increasing concns. of levamisole (0.1 to 100 μg/mL). Levamisole had no consistent effect on induction of 2',5'-oligoadenylate synthetase or indoleamine -2,3-dioxygenase activity, or production of tumor necrosis factor. Levamisole had no effect on monocyte cytotoxicity or expression of HLA-DR, HLA-DQ, HLA-DP, and the Fc receptor. Similarly, levamisole had no significant effect on NK or LAK cytotoxicity or the immunol. activation of T-lymphocytes, assessed by expression of CD3, CD4, CD8, CD16, CD25, and CD56. Proliferation of lymphocytes from normal donors, patients with benign polyps, and patients with malignancies, with or without IL-2 or irradiated LS174T cells, was not significantly increased overall. No

significant enhancement in the expression of three tumor-associated antigens (880364, NRCO-4, and ING-1) and the intercellular adhesion mol.-1 (ICAM-1) antigen on 4 human cancer cell lines was observed following in vitro exposure to levamisole. Thus, levamisole is not a potent modulator of the immune parameters examined, and the mechanism behind the unique clin. interaction between levamisole and 5-fluorouracil in colorectal carcinoma remains to be identified.

L3 ANSWER 42 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1991:551259 CAPLUS
DOCUMENT NUMBER: 115:151259
TITLE: Effects of melatonin on the cell cycle kinetics and "estrogen-rescue" of MCF-7 human breast cancer cells in culture
AUTHOR(S): Cos, Samuel; Blask, David E.; Lemus-Wilson, Athena; Hill, Anna B.
CORPORATE SOURCE: Coll. Med., Univ. Arizona, Tucson, AZ, 85724, USA
SOURCE: Journal of Pineal Research (1991), 10(1), 36-42
CODEN: JPRSE9; ISSN: 0742-3098
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Melatonin has been shown to have a direct inhibitory action on the proliferation of estrogen-responsive MCF-7 human breast cancer cells in culture. This inhibitory effect might be exerted on the G1 phase of the cell cycle, thus causing a transition delay into the S phase. In order to further verify this hypothesis the ability of estradiol to "rescue" MCF-7 cells from melatonin inhibition was tested and the potential of this indoleamine to block the ability of estradiol to rescue the cells from tamoxifen inhibition. Following five days of incubation, melatonin (10-9M) increased the fraction of cells in G1 of the cell cycle while simultaneously causing a 50% reduction in the proportion of cells in S phase. The antiproliferative effect of melatonin (10-5M) was prevented by the simultaneous treatment of the cells with estradiol (10-8M) in clonogenic soft agar culture, or reversed by the addition of estradiol to cells previously incubated with and inhibited by melatonin (10-9M) in monolayer culture. Addnl., melatonin blocked the estrogen-rescue of tamoxifen-inhibited cells in both types of culture systems. These results support the hypothesis that the antiproliferative effect of melatonin, like tamoxifen, is cell cycle specific by causing a G1-S transition delay. These results also indicate an important interaction of melatonin with estrogen-mediated mechanisms of MCF-7 cell proliferation.

L3 ANSWER 43 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:550478 CAPLUS
DOCUMENT NUMBER: 113:150478
TITLE: IFN-γ is the inducer of indoleamine 2,3-dioxygenase in allografted tumor cells undergoing rejection
AUTHOR(S): Takikawa, Osamu; Habara-Ohkubo, Akemi; Yoshida, Ryotaro
CORPORATE SOURCE: Dep. Cell Biol., Osaka Biosci. Inst., Suita, 565, Japan
SOURCE: Journal of Immunology (1990), 145(4), 1246-50
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The depletion of an essential amino acid, tryptophan, caused by induction of indoleamine 2,3-dioxygenase (IDO), has been shown to be a mechanism involving self-defense against inhaled microorganisms

and tumor growth. Recently, it was reported that the IDO is (.apprx.50-fold) induced in allografted tumor (3-methylcholanthrene-induced ascites type tumor cells) cells undergoing rejection, and that the enzyme is induced by factor(s) released through the interaction of allografted tumor cells with infiltrating leukocytes. The culture supernatant of infiltrating leukocytes, which were harvested on day 7 after tumor transplantation, induced the highest IDO activity in the tumor cells. The inducer activity was completely neutralized by the addition of antibody to IFN-γ but not by antibody to IFN-α/β. Approx. 6 U/mL of IFN-γ was detected by an ELISA assay in the 12-h culture supernatant with 2 + 106 leukocytes/mL, and rIFN-γ at 6 U/mL induced IDO in 3-methylcholanthrene-induced ascites type tumor cells to the same extent as IFN-γ in the culture supernatant. Moreover, i.p. administration of antibody to IFN-γ almost completely inhibited the induction of IDO in the allografted tumor cells. Thus, the factor responsible for IDO induction in the allografted tumor cells is IFN-γ.

L3 ANSWER 44 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:459786 CAPLUS
DOCUMENT NUMBER: 113:59786
TITLE: Preparation of carbocyclic adenine nucleoside analogs as virucides and antitumor agents
INVENTOR(S): Kitagawa, Isao
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| JP 02017190 | A | 19900122 | JP 1988-166523 | 19880704 <-- |

PRIORITY APPLN. INFO.: JP 1988-166523 19880704
OTHER SOURCE(S): MARPAT 113:59786
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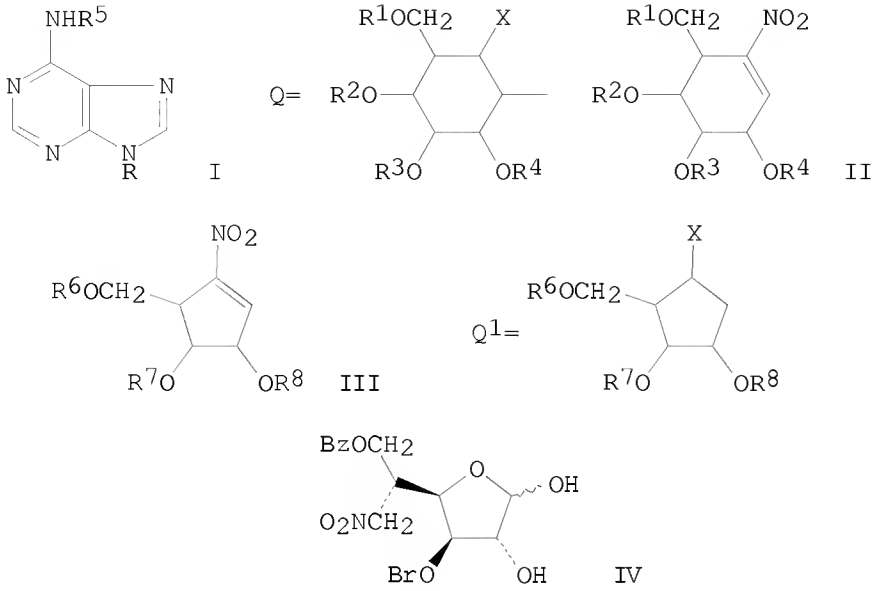


AB The title compds. (I; R = Q, Q1; X = H; R1 - R4, R6 - R8 = H, protecting group; R5 = H, protecting group), having strong antitumor and antiviral activity (no data), are prepared in good yields by addition reaction of nitrohexene and nitropentene derivs. II and III (R1 - R4, R6 - R8 = protecting group) with N-protected adenines and denitration of the resulting I (R = Q, Q1; X = NO2; R1 - R8 = protecting group). Thus, treatment of a dehydrofuranose (IV; Bn = CH2Ph) with KF and 18-crown-6 ether in DMF at 23° for 3 h gave, after acetylation, pseudo-D-gluco-II (R1 = Bz, R2 = R4 = Ac, R3 = Bn) which was stirred 1 h at 0° with I (R = H, R5 = Bz) in DMF in the presence of KF and 18-crown-6 to give pseudo-D-gluco-I (R = Q, = NO2, R1 = R5 = Bz, R2 = R4 = Ac, R3 = Bn). Denitration of the latter with Bn3BH and azobisisobutyronitrile in benzene at 80° for 3 h gave pseudo-D-gluco-I (R = Q, X = H, R1 = R5 = Bz, R2 = R4 = Ac, R3 = Bn) which was saponified with 1% NaOH/MeOH and then debenzylated with Na in NH3(l)/THF at -78° to give 9-pseudo-β-D-glucopyranosyladenine, i.e. pseudo-D-gluco-I (R = Q, X = R1 = R5 = H). Also prepared were pseudo-L-ido-I (R = X, X = R1 - R5 = H) and pseudo-L-xylo-I (R = Q1, X = R1 - R5 = H).

L3 ANSWER 45 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:53442 CAPLUS
DOCUMENT NUMBER: 112:53442
TITLE: Synergistic effects of phorbol ester and INF-γ on the induction of indoleamine 2,3-dioxygenase in THP-1 monocytic leukemia cells
AUTHOR(S): Edelstein, Mark P.; Ozaki, Yoshisuke; Duch, David S.
CORPORATE SOURCE: Dep. Med. Biochem., Wellcome Res. Lab., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Immunology (1989), 143(9), 2969-73
CODEN: JOIMA3; ISSN: 0022-1767
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO) is a flavin-dependent enzyme which uses superoxide anion as a cosubstrate to catalyze the decyclization of the pyrrole ring of L-tryptophan to form

formylkynurenine. This enzyme is induced in some tumor cells after treatment with IFN-γ. The mechanism of induction of IDO in tumor cells by IFN-γ was studied in THP-1 human monocytic leukemia cells. Before the addition of IFN-γ no IDO could be detected in these cells. Treatment of THP-1 cells with IFN-γ produced an induction of IDO, with peak activity occurring 72 to 96 h after addition of IFN-γ. Because phorbol esters are known to induce many enzymes in cells, most likely through the activation of protein kinase C, the effects of PMA on the induction of IDO were determined PMA potentiated the IFN-γ-induced elevation of IDO, but by itself, was unable to induce enzyme activity. Maximum induction of IDO in the presence of PMA and IFN-γ was obtained by preexposure of the cells to PMA for 78 h before the addition of IFN-γ. Maximum induction of IDO after the addition of IFN-γ occurred 24-48 h after addition of the cytokine to the culture medium. However, the induction of IDO does not appear to be potentiated through the activation of protein kinase C, because the addition of the protein kinase C inhibitor H-7 had no effect on the induction of IDO when the cells were exposed to PMA and IFN-γ. Moreover, diacylglycerol was unable to replace PMA in these studies. Studies with cAMP and cGMP analogs suggest a role for these compds. in the regulation of IDO expression.

L3 ANSWER 46 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1990:34224 CAPLUS
DOCUMENT NUMBER: 112:34224
TITLE: The effects of human interferons and retinoic acid on human neuroblastoma cells. Morphological differentiation and induction of 2',5'-oligoadenylate synthetase, protein kinase and indoleamine dioxygenase
AUTHOR(S): Hiratani, Hajime
CORPORATE SOURCE: Dep. Microbiol., Kyoto Prefect. Univ. Med., Kyoto, Japan
SOURCE: Kyoto-furitsu Ika Daigaku Zasshi (1989), 98(9), 961-80
CODEN: KFIZAO; ISSN: 0023-6012
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB Human interferon-γ (HuIFN-γ), dibutyryl cAMP, and bromodeoxyuridine were screened for the ability to induce morphol. differentiation of a human neuroblastoma (NB) GOTO cell line, in vitro. In particular, HuIFN-γ induced both the extension of complicatedly branched neurites and the formation of giant cells in NB cells. Although with the treatment of retinoic acid (RA) the morphol. differentiation did not occur, with the combination of HuIFN-γ and RA, intensified effects were shown. The 2'-5'-oligoadenylate synthetase (2-5AS), which is dependent on double stranded RNA (ds-RNA), was induced in NB cells by HuIFN-γ treatment. However, its activity in the HuIFN-γ-treated NB cells was far less than that in HuIFN-α- or HuIFN-β-treated NB cells. HuIFN-γ induced also ds-RNA-dependent protein kinase (PK) in NB cells. However, its activity was far less than that in HuIFN-α- or HuIFN-β-treated cells, as well as 2-5AS. RA intensified the effects of HuIFN-γ in terms of morphol. differentiation, but it did not increase the activity of 2-5AS and PK. Induction of indoleamine dioxygenase (IDO) activity was observed specifically in HuIFN-γ-treated NB cells. Since tryptophan was degraded to N-formyl kynurenine by the induction of IDO, the degraded tryptophan was complemented by the addnl. tryptophan to the culture medium. However, the induction of morphol. differentiation by HuIFN-γ treatment could not be inhibited. N-Formyl kynurenine or kynurenine, which are the catabolites of

tryptophan, did not induce the morphol. differentiation on NB cells. Thus, the induction of morphol. differentiation by HuIFN-γ is not correlated to the induction of the enzymic activities such as 2-5AS, PK, and IDO.

L3 ANSWER 47 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:495020 CAPLUS
DOCUMENT NUMBER: 111:95020
TITLE: Interferons and indoleamine 2,3-dioxygenase: role in antimicrobial and antitumor effects
AUTHOR(S): Carlin, J. M.; Ozaki, Y.; Byrne, G. I.; Brown, R. R.; Borden, E. C.
CORPORATE SOURCE: Med. Sch., Univ. Wisconsin, Madison, WI, 53706, USA
SOURCE: Experientia (1989), 45(6), 535-41
CODEN: EXPEAM; ISSN: 0014-4754
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 71 refs. Indoleamine 2,3-dioxygenase (IDO ) is an interferon (IFN)-induced protein that initiates the metabolism of tryptophan along the kynurenine pathway. Although IDO can be induced by IFN-γ in many cell types, only mononuclear phagocytes have been shown to be induced to decyclize tryptophan by all three IFN classes. Since tryptophan is an essential amino acid necessary for a variety of metabolic processes, depletion of available tryptophan may be an important mechanism for control of rapidly-dividing microbial pathogens and tumors. The effects of IFN-induced IDO on prokaryotic and eukaryotic pathogens, as well as on a variety of tumor cell lines, are described.

L3 ANSWER 48 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:110482 CAPLUS
DOCUMENT NUMBER: 110:110482
TITLE: Superoxygenase
AUTHOR(S): Yoshida, Ryotaro
CORPORATE SOURCE: Dep. Cell Biol., Osaka Biosci. Inst., Suita, Japan
SOURCE: Tanpakushitsu Kakusan Koso (1988), 33(16), 3048-53
CODEN: TAKKAJ; ISSN: 0039-9450
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 24 refs., of the enzymic characterization of indoleamine oxygenase, with discussions of its mechanism of induction and its relation to antitumor activity.

L3 ANSWER 49 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:129837 CAPLUS
DOCUMENT NUMBER: 108:129837
TITLE: Induction of indoleamine 2,3-dioxygenase: a mechanism of the antitumor activity of interferon γ
AUTHOR(S): Ozaki, Yoshisuke; Edelstein, Mark P.; Duch, David S.
CORPORATE SOURCE: Dep. Med. Biochem., Wellcome Res. Lab., Research Triangle Park, NC, 27709, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1988), 85(4), 1242-6
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The antiproliferative effects of interferon α (IFN-α) and interferon γ (IFN-γ) were found to be cell-dependent. Among the human cell lines examined, IFN-γ had a greater antiproliferative

effect against cell lines that exhibited induction of indoleamine 2,3-dioxygenase, such as the KB oral carcinoma or WiDr colon adenocarcinoma, than against those that lacked the enzyme activity, such as the SW480 colon adenocarcinoma or NCI-H128 small-cell lung carcinoma. Induction of this dioxygenase showed a clear temporal relationship with increased metabolism of L-tryptophan and the depletion of this amino acid in the culture medium. While 70-80% of D-tryptophan remained in the medium of IFN-α- or vehicle-treated cells, virtually all of this amino acid was depleted in the medium of the IFN-γ-treated group following 2-3 days of culture. Supplementing the growth medium with addnl. L-tryptophan reversed the antiproliferative effect of IFN-γ against KB cells in a dose- and time-dependent manner. The antiproliferative effects of IFN-α and IFN-γ on SW480 and NCI-H128 cells, which are independent of the dioxygenase activity, and the inability of added L-tryptophan to reverse the effects of IFN-γ in WiDr cells suggest multiple mechanisms of action of the IFNs. The antiproliferative effect of IFN-γ through induction of indoleamine 2,3-dioxygenase, with a consequent L-tryptophan deprivation, is an effective means of regulating cell growth.

L3 ANSWER 50 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1988:110590 CAPLUS
DOCUMENT NUMBER: 108:110590
TITLE: Mechanism of interferon-γ action. Characterization of indoleamine 2,3-dioxygenase in cultured human cells induced by interferon-γ and evaluation of the enzyme-mediated tryptophan degradation in its anticellular activity
AUTHOR(S): Takikawa, Osamu; Kuroiwa, Takekiyo; Yamazaki, Fumio; Kido, Ryo
CORPORATE SOURCE: Dep. Biochem., Wakayama Med. Coll., Wakayama, 640, Japan
SOURCE: Journal of Biological Chemistry (1988), 263(4), 2041-8
CODEN: JBCHA3; ISSN: 0021-9258
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Induction by interferon-γ of indoleamine 2,3-dioxygenase (a tryptophan degradation enzyme) was examined in human cell lines. The enzyme induction was demonstrated in 7 of the 11 cell lines. The induced enzyme in each of the 7 cell lines was identical to the enzyme purified from human placenta, as evidenced by immunoblot anal. with a monoclonal antibody specific to the placental one. The extent of the induction varied largely with the cell line; a relatively high induction was observed with HEL (lung fibroblasts), NY (osteosarcoma), and A-431 (epidermoid carcinoma). The enzyme induction was dependent on the concentration of interferon-γ and occurred 12-18 h after addition of interferon-γ to the cultures. Interferon-α or -β was completely ineffective. Interferon-γ inhibited the growth of the 7 cell lines observed with the enzyme induction, and this growth inhibition was accompanied with a complete deletion of tryptophan (<1 μM) in the culture medium by the induction of the enzyme. For 2 of these cell lines, the inhibition was partially reversed by an addition of exogenous tryptophan to the medium. Thus, the growth inhibition by interferon-γ can in part be explained by the tryptophan depletion in the medium caused by the enzyme induction.

L3 ANSWER 51 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1987:509832 CAPLUS
DOCUMENT NUMBER: 107:109832
TITLE: Growth-inhibiting effect of crude pineal extracts on

human melanoma cells in vitro is different from that of known synthetic pineal substances

AUTHOR(S): Bartsch, Hella; Bartsch, C.; Noteborn, H. P. J. M.; Flehmig, B.; Ebels, I.; Salemink, C. A.

CORPORATE SOURCE: Inst. Hyg., Univ. Tuebingen, Tuebingen, D-7400, Fed. Rep. Ger.

SOURCE: Journal of Neural Transmission (1972-1989) ( 1987), 69(3-4), 299-311
CODEN: JNTMAH; ISSN: 0300-9564

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of a number of synthetic indoleamines, pteridines, β-carbolines, arginine vasotocin, and crude exts. from rat and ovine pineal glands on human melanoma cells were studied in vitro. The identified pineal substances as well as some of their analogs showed an inhibitory effect only at nonphysiol. high concns. However, crude pineal exts. were more active than the synthetic pineal substances tested. They contain a compound which may have a tumor-inhibiting potency comparable to that of methotrexate but with a different mechanism of action.

L3 ANSWER 52 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1986:218611 CAPLUS

DOCUMENT NUMBER: 104:218611

ORIGINAL REFERENCE NO.: 104:34477a,34480a

TITLE: Efficient breakage of DNA apurinic sites by the indoleamine related 9-amino-ellipticine

AUTHOR(S): Malvy, Claude; Prevost, Philippe; Gansser, Charles; Viel, Claude; Paoletti, Claude

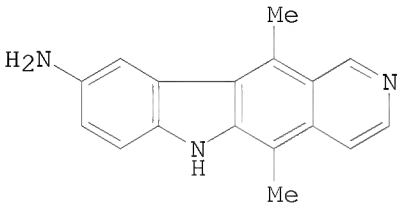
CORPORATE SOURCE: INSERM, Villejuif, 94800, Fr.

SOURCE: Chemico-Biological Interactions (1986), 57(1), 41-53
CODEN: CBINA8; ISSN: 0009-2797

DOCUMENT TYPE: Journal

LANGUAGE: English

GI

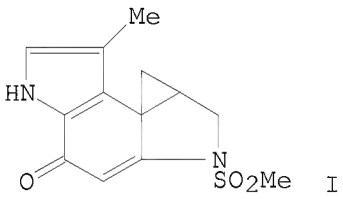



I

AB The aromatic amine, 9-NH2-ellipticine (I) [54779-53-2], is a synthetic DNA intercalating derivative of the antitumor agent ellipticine, which breaks circular DNA containing apurinic sites. This breakage is inhibited when the apurinic (AP) sites are reduced. The concentration of 9-NH2-ellipticine required to get a significant effect (0.1 μM) is the lowest known among chemical which induce the same breakage reaction. Comparison with the action of structurally related amines shows that the amino-indole structure is specific for AP sites. The ability of ellipticine derivs. to induce breakage in DNA containing apurinic sites is related to the nucleophile substituent in position 9. Two ellipticine derivs. with known antitumor activity, BD 40 [65222-35-7] and 9-OH-ellipticine [51131-85-2], were able to break purified DNA at apurinic sites.

L3 ANSWER 53 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1984:421392 CAPLUS
DOCUMENT NUMBER: 101:21392
ORIGINAL REFERENCE NO.: 101:3374h,3375a
TITLE: Role of indoleamine 2,3-dioxygenase in the defense mechanism against tumor growth
AUTHOR(S): Yoshida, Ryotaro; Takikawa, Osamu; Yasui, Hiroaki; Hayaishi, Osamu
CORPORATE SOURCE: Fac. Med., Kyoto Univ., Kyoto, 606, Japan
SOURCE: Prog. Tryptophan Serotonin Res., Proc. - Meet. Int. Study Group Tryptophan Res. ISTRY, 4th (1984), Meeting Date 1983, 513-16. Editor(s): Schlossberger, Hans Georg. de Gruyter: Berlin, Fed. Rep. Ger.
CODEN: 51OLA5
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Indoleamine 2,3-dioxygenase (IDO) was induced in tumor cells injected i.p. into allogenic strains of mice but not in tumor cells injected into syngeneic animals. Studies suggested that a decrease in the intracellular concentration of tryptophan, the substrate for IDO, caused tumor growth inhibition.

L3 ANSWER 54 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1981:532714 CAPLUS
DOCUMENT NUMBER: 95:132714
ORIGINAL REFERENCE NO.: 95:22223a,22226a
TITLE: Synthesis of the left-hand segment of the antitumor agent CC-1065
AUTHOR(S): Wierenga, Wendell
CORPORATE SOURCE: Upjohn Co., Kalamazoo, MI, 49001, USA
SOURCE: Journal of the American Chemical Society (1981), 103(18), 5621-3
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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AB A new, highly potent antitumor agent has recently been shown to be a trimer of pyrroloindoles, two of which are the same and have been prepared by Komoto et al. (1979). The unique segment, cyclopropylpyrroloindole I, has been prepared to isolate its biol. activity. Thus, 4-chloro-3-nitroanisole is converted to the indoline portion through a reductive cyclization. This is regiospecifically converted to the aminoindoline on which the methylindolic portion is elaborated via the Gassman indole chemical Ultimate intramol. para alkylation gave I.

L3 ANSWER 55 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1978:526647 CAPLUS
DOCUMENT NUMBER: 89:126647
ORIGINAL REFERENCE NO.: 89:19571a,19574a
TITLE: Uptake of biogenic amines by glial cells in culture.

I. A neuronal-like transport system for serotonin

AUTHOR(S): Suddith, R. L.; Hutchison, H. T.; Haber, B.

CORPORATE SOURCE: Mar. Biomed. Inst., Univ. Texas Med. Branch, Galveston, TX, USA

SOURCE: Life Sciences (1978), 22(24), 2179-87
CODEN: LIFSAK; ISSN: 0024-3205

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Rat C6 astrocytoma cells take up serotonin (5HT) via a high-affinity carrier-mediated system with Km = 1 μM, and a 2nd component of lower affinity. This high-affinity 5HT transport system was rapid, concentrative, and highly Na and temperature dependent. Chlorimipramine and Lilly 110140 preferentially blocked the glial 5HT but not norepinephrine uptake. This preferential inhibition had previously been shown for synaptosomes and brain slices. Norepinephrine, and to a lesser extent dopamine, blocked the glial 5HT uptake, suggesting a partial overlap between the catecholamine and indoleamine glial carrier systems. 5-Hydroxy-, but not 6-hydroxydopamine inhibited the high-affinity 5HT transport in glia. A variety of ring hydroxylated indoleamine analogs blocked this glial 5HT transport; of the compds. tested, 5,7-dihydroxytryptamine was the least effective inhibitor. Phenylethylamine and its O-methylated derivs. blocked synaptosomal and glial 5HT transport equally well. Thus, cultured C6 cells used as models of glia may possess a 5HT transport system which kinetically and pharmacol. resembles a neuronal 5HT transport system.

L3 ANSWER 56 OF 56 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1978:105410 CAPLUS

DOCUMENT NUMBER: 88:105410

ORIGINAL REFERENCE NO.: 88:16545a,16548a

TITLE: 7-Substituted -7H-pyrrolo[3,2-f]quinazoline-1,3-diamines

INVENTOR(S): Ledig, Kurt Willi

PATENT ASSIGNEE(S): American Home Products Corp., USA

SOURCE: Ger. Offen., 112 pp.
CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE | |
|---|---|---|---|---|---|
| DE 2731039 | A1 | 19780119 | DE 1977-2731039 | 19770708 | <-- |
| ZA 7703939 | A | 19790228 | ZA 1977-3939 | 19770629 | <-- |
| GB 1579678 | A | 19801119 | GB 1977-27487 | 19770630 | <-- |
| AU 7726687 | A | 19790104 | AU 1977-26687 | 19770701 | <-- |
| AU 507828 | B2 | 19800228 | | | |
| BE 856647 | A1 | 19780109 | BE 1977-179213 | 19770708 | <-- |
| DK 7703099 | A | 19780110 | DK 1977-3099 | 19770708 | <-- |
| NL 7707658 | A | 19780111 | NL 1977-7658 | 19770708 | <-- |
| FR 2357563 | A1 | 19780203 | FR 1977-21232 | 19770708 | <-- |
| FR 2357563 | B1 | 19830311 | | | |
| CH 634069 | A5 | 19830114 | CH 1977-8506 | 19770708 | <-- |
| IN 147488 | A1 | 19800315 | IN 1977-CA1610 | 19771115 | <-- |
| IN 147815 | A1 | 19800705 | IN 1979-CA874 | 19790823 | <-- |
| CH 635842 | A5 | 19830429 | CH 1982-2893 | 19820510 | <-- |
| CH 636616 | A5 | 19830615 | CH 1982-2894 | 19820510 | <-- |

PRIORITY APPLN. INFO.:

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|---|---|---|
| US 1976-704001 | A | 19760709 |
| US 1976-704002 | A | 19760709 |
| GB 1976-53821 | A | 19761223 |
| US 1977-784987 | A | 19770406 |

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| IE 1976-2853 | A | 19761231 |
| US 1977-78987 | A | 19770406 |
| CH 1977-8506 | A | 19770708 |
| IN 1977-CA1610 | A1 | 19771115 |

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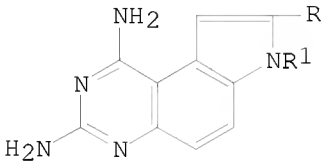

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AB Pyrroloquinazolinediamines I (R = H, Me, Ph, Cl; R1 = H, alkyl, cycloalkylmethyl, phenylalkyl, optionally substituted benzyl or Ph, naphthylmethyl, heterocyclylmethyl, heterocyclyl)(109 compds.) were prepared Thus, 5-aminoindole-HCl was condensed with HN(CN)2 to give I (R = R1 = H), which had a min. inhibitory concentration Staphylococcus aureus 31.3 mg/mL. Other I also showed antimalarial and antileukemic activity.

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